Oral Hypoglycaemic Agents and Insulin

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To Start With, Some Statistics

- The incidence of diabetes has risen from 1.8 to 3.3 per 1000 person years between 1994 and 2003
- The prevalence is now 2.7 per 1000 person years
- Estimated at 4.67% of the population has either diagnosed or undiagnosed diabetes

Yorkshire and Humber Public Health Observatory March 2006

To Start With, Some More Statistics

- Type 2 diabetes accounts for 92% of all cases in the UK
- The incidence of type 2 diabetes doubled between 1994 and 2003
- Diabetes reduces life expectancy by 15 years for type 1 and 5 or 7 years in type 2 (M/F)

Yorkshire and Humber Public Health Observatory March 2006

To Start With, Some More Statistics

- Diabetes accounts for 5% of all NHS expenditure – in 2002 £1.3bn
- It accounts for 9% of all hospital costs
- Drugs used in the treatment of diabetes account for the second biggest cost

Myths in the Treatment of Diabetes

- The treatment of diabetes is straightforward and response to treatment is ready and predictable
- The majority of people with diabetes are mainly supervised in secondary care
- Community services have the capacity to absorb work shifted from specialist services
- Practitioners in the community possess the equivalent knowledge and skills to those based in specialist diabetes centres
- Major relocation of resources will not undermine specialist centres which deliver speciality services to in-patients, as well as out-patients
- The shift of care will produce better clinical outcomes

Munro et al Pract Diab Int 2005;22(5):153-4

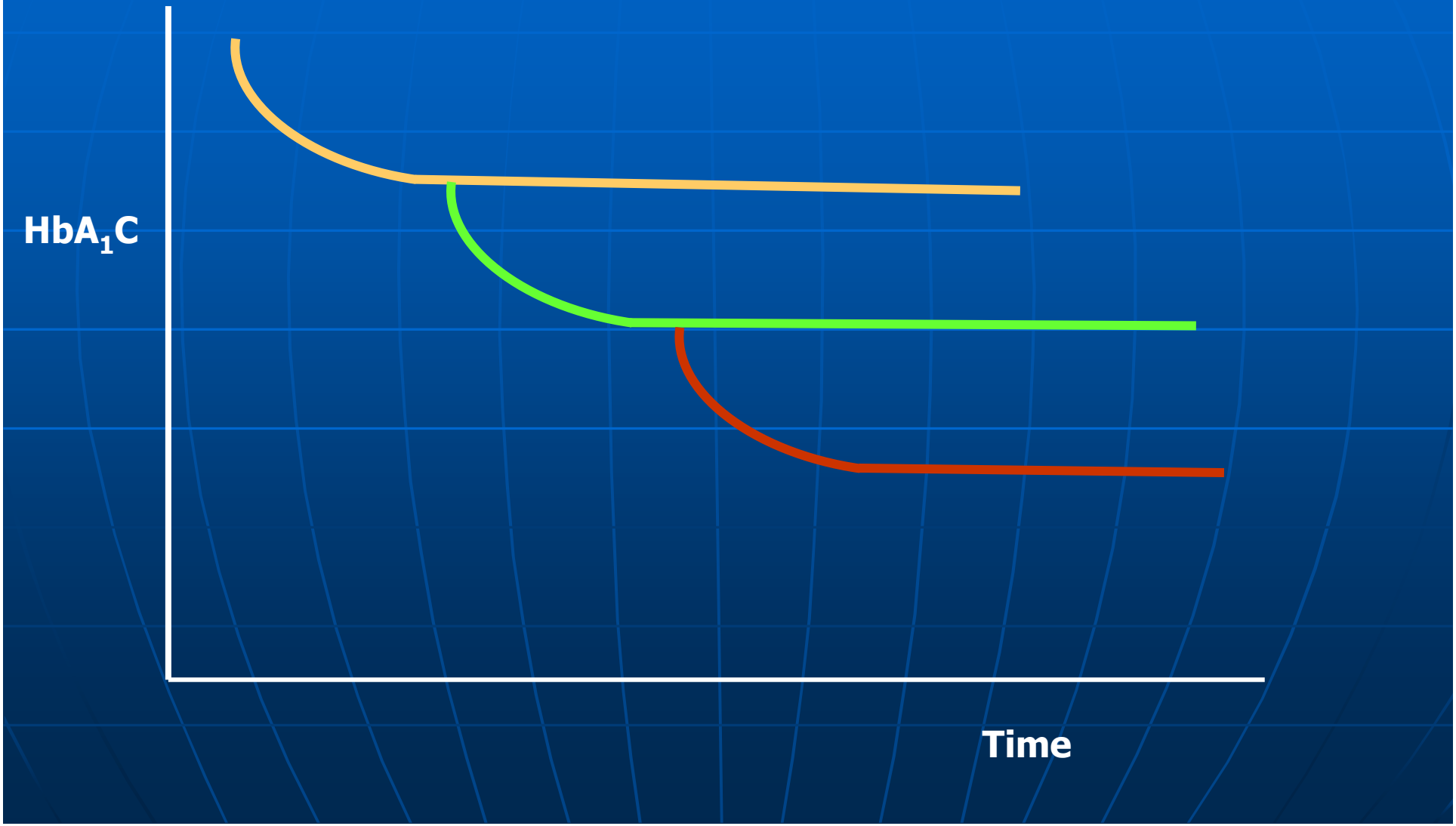
Choices, Choices

- Oral hypoglycaemic agents 
- Insulins 

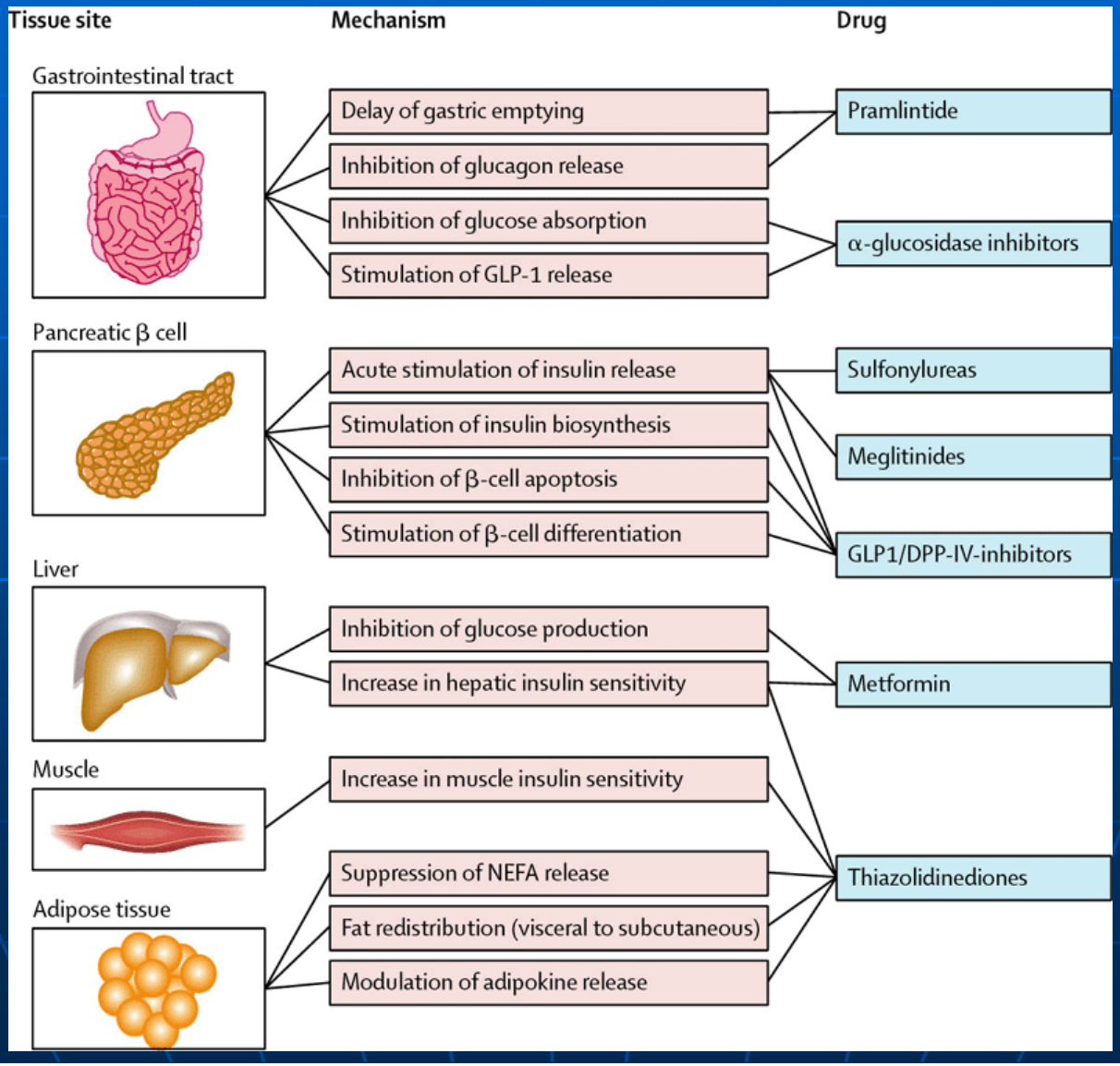
Hypoglycaemic Agents

- α glucosidase inhibitors
- Metaglinides
- Metformin
- Sulphonylureas
- Thiazolidindiones
- GLP – 1 analogues
- DPP IV inhibitors
- SGLT2 inhibitors

Their Effects Are Additive



Oral Agents and Site of Action



Oral Hypoglycaemic Agents

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Acarbose

- Marginal benefit – no overall effect on hyperinsulinaemia or insulin sensitivity
- Best for individuals with normal fasting glucose but high postprandial glucose levels
- Maximum HbA_1C reduction of 0.75%
- Can be used in combination with insulin, metformin or SU's

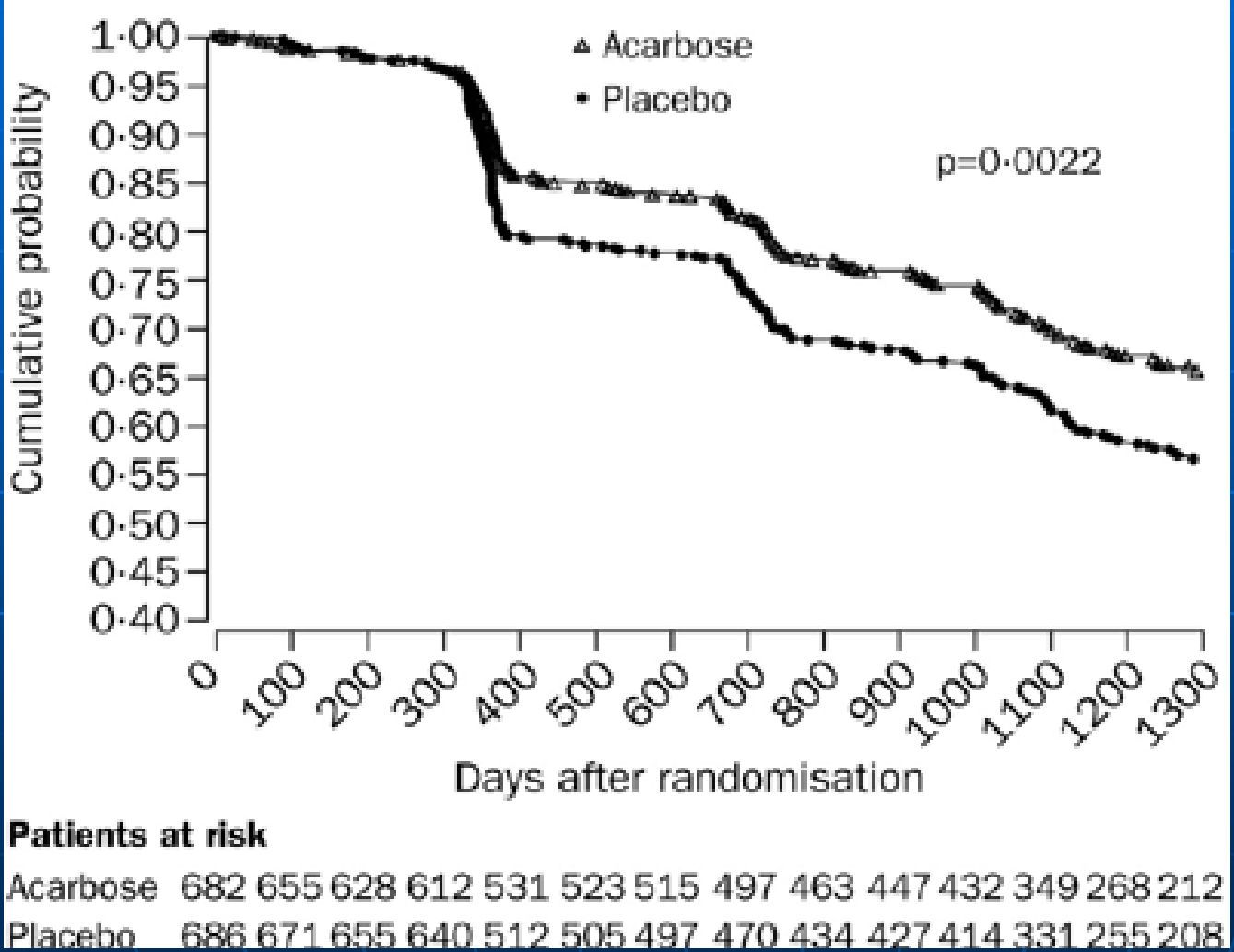
Acarbose

- GI side effects abound therefore dose gradually built up
- Contraindicated in inflammatory bowel disease, cirrhosis, severe renal impairment, history of abdominal surgery

Acarbose

- STOP-NIDDM trial (Lancet 2002)
- 714 patients with impaired glucose tolerance randomised to 100mg tds acarbose and 715 to placebo for a mean of 3.3 years

Acarbose



Compared with placebo:

48% reduction in incidence of new onset Type 2 diabetes

42% increase in incidence of normalised OGTT

Effect of acarbose and placebo on cumulative probability of remaining free of diabetes over time

Chiasson et al Lancet 2002 359:2072-2077

Acarbose - Reasons for Premature Discontinuation

	Acarbose (n=714)	Placebo (n=715)
All adverse events	136 (19%)	37 (5%)
Gastrointestinal	93 (13%)	18 (3%)
Flatulence	67 (9%)	5 (1%)
Diarrhoea	39 (5%)	6 (1%)
Abdominal pain	23 (3%)	4 (1%)
Other	9 (1%)	7 (1%)

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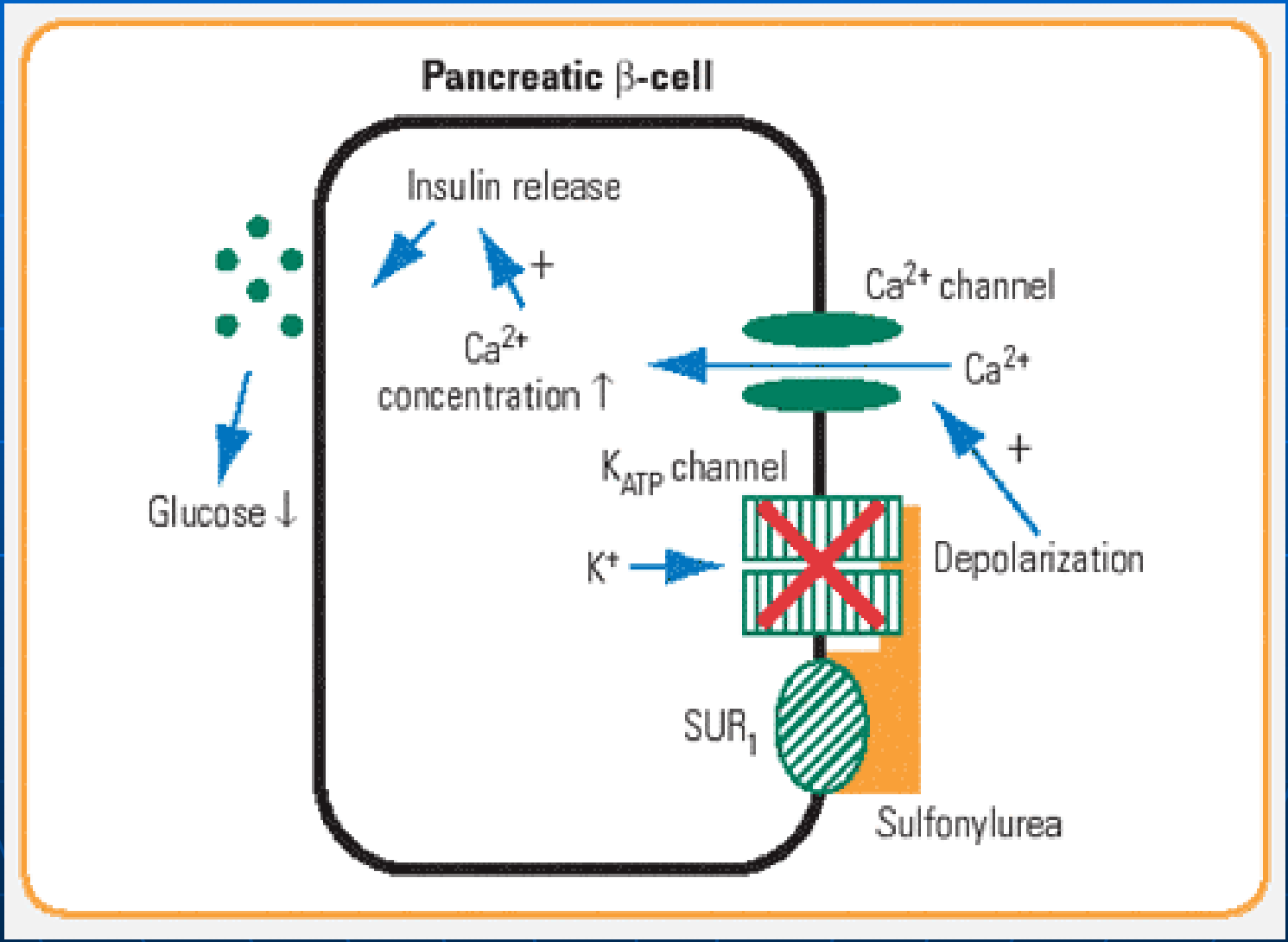
Metaglinides

- Repaglinide and Nateglinide
  - First introduced in 1998
  - Work by binding to the sulphonylurea receptor and 'squeezing' the β cell to release insulin
  - They stimulate first-phase insulin release in a glucose-sensitive manner

Metaglinides



Metaglinides

- Short acting
- Taken only with meals
- Marginal benefit
- Best for individuals with normal fasting glucose but high postprandial glucose levels
- Maximum HbA_1C reduction of 1.0%

Hypoglycaemic Agents

- α glucosidase inhibitors
- Metaglinides
- Metformin
- Sulphonylureas
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- GLP – 1 analogues
- DPP IV inhibitors
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Metformin

Derived from French lilac (***Galega officinalis)***

Metformin

- Used since medieval times in some form or other
- Should be the first line oral hypoglycaemic agent for almost all individuals with type 2 diabetes
- BMI is no longer an issue

Ungar G, Freedman L, Shapira S. Pharmacological studies of a new oral hypoglycaemic drug. Proceedings of the Society for Experimental Biology and Medicine. 1957;95:190-192

Metformin

- Works by decreasing hepatic gluconeogenesis, decreasing gut glucose uptake and increasing peripheral insulin sensitivity
- Relies on adequate β cell function
- Weight neutral
- Can be used in combination with other oral agents or insulin

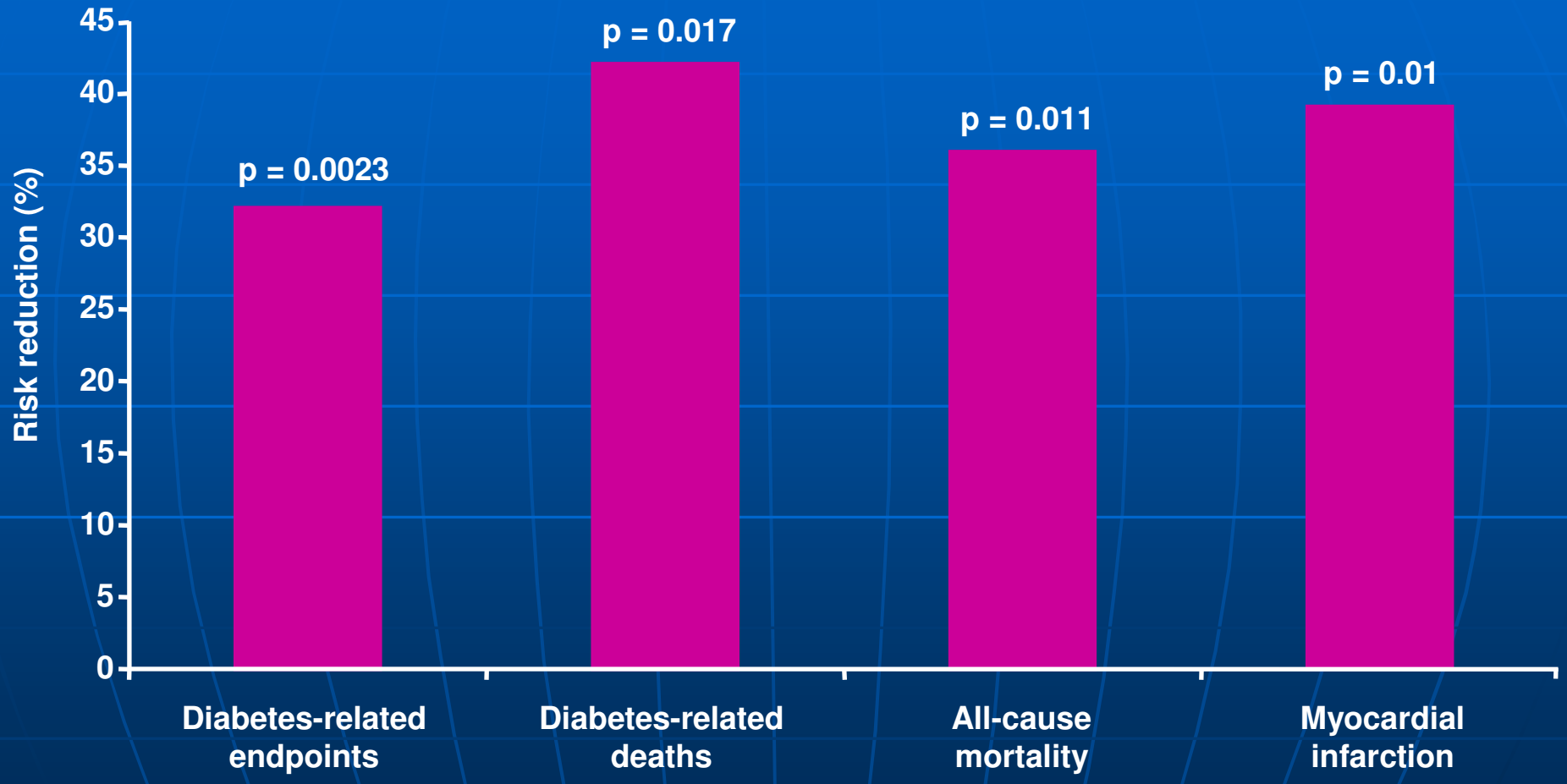
Metformin

- GI disturbance is common so dose titrated
- Maximum HbA_1C reduction is 1.5%

Metformin

- Hypoglycaemia is NOT a side effect of treatment
- Avoid in conditions predisposing to renal insufficiency and/or hypoxia
- Lactic acidosis is a theoretical risk

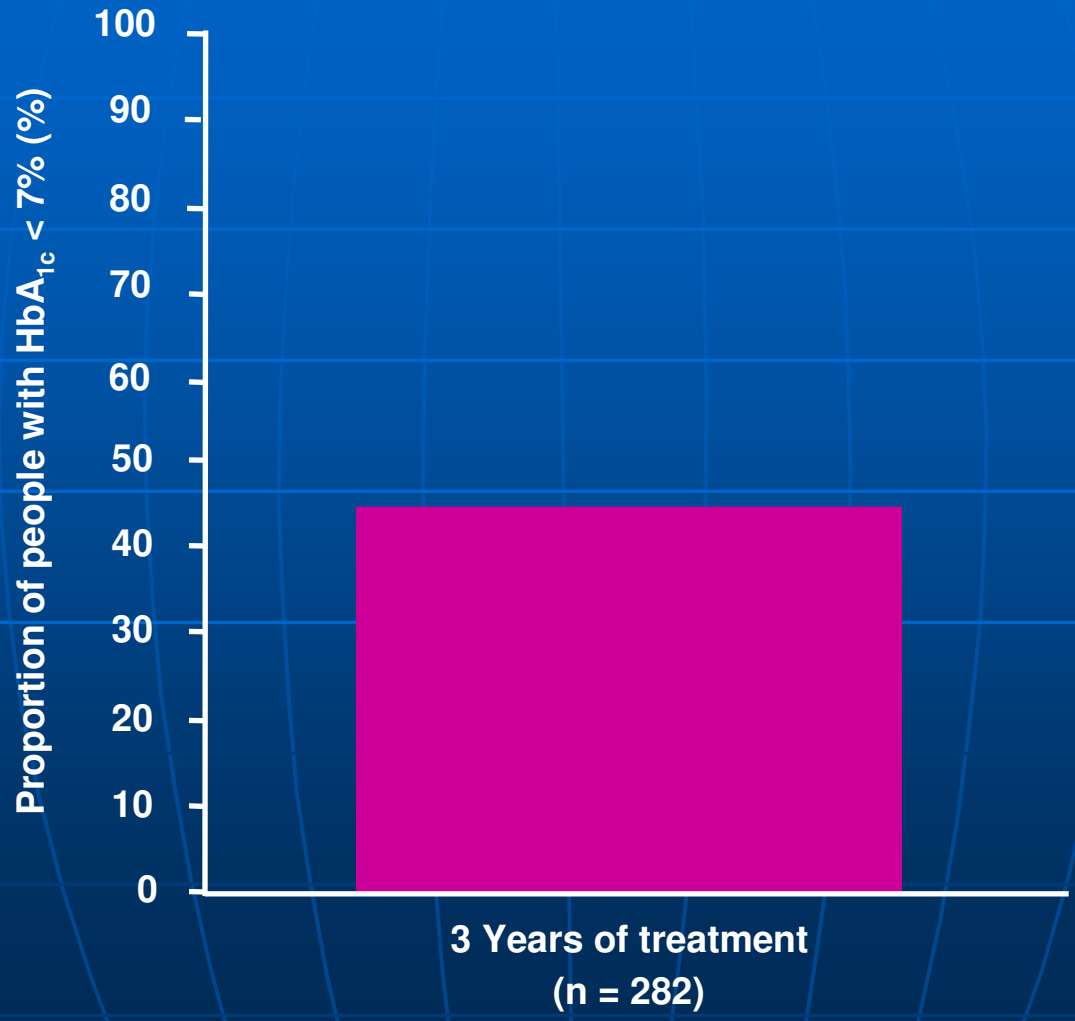
Preventing Cardiovascular Complications UKPDS: Benefits of Metformin in Overweight Type 2 Diabetes Patients



*Compared with conventional treatment group (primarily diet)

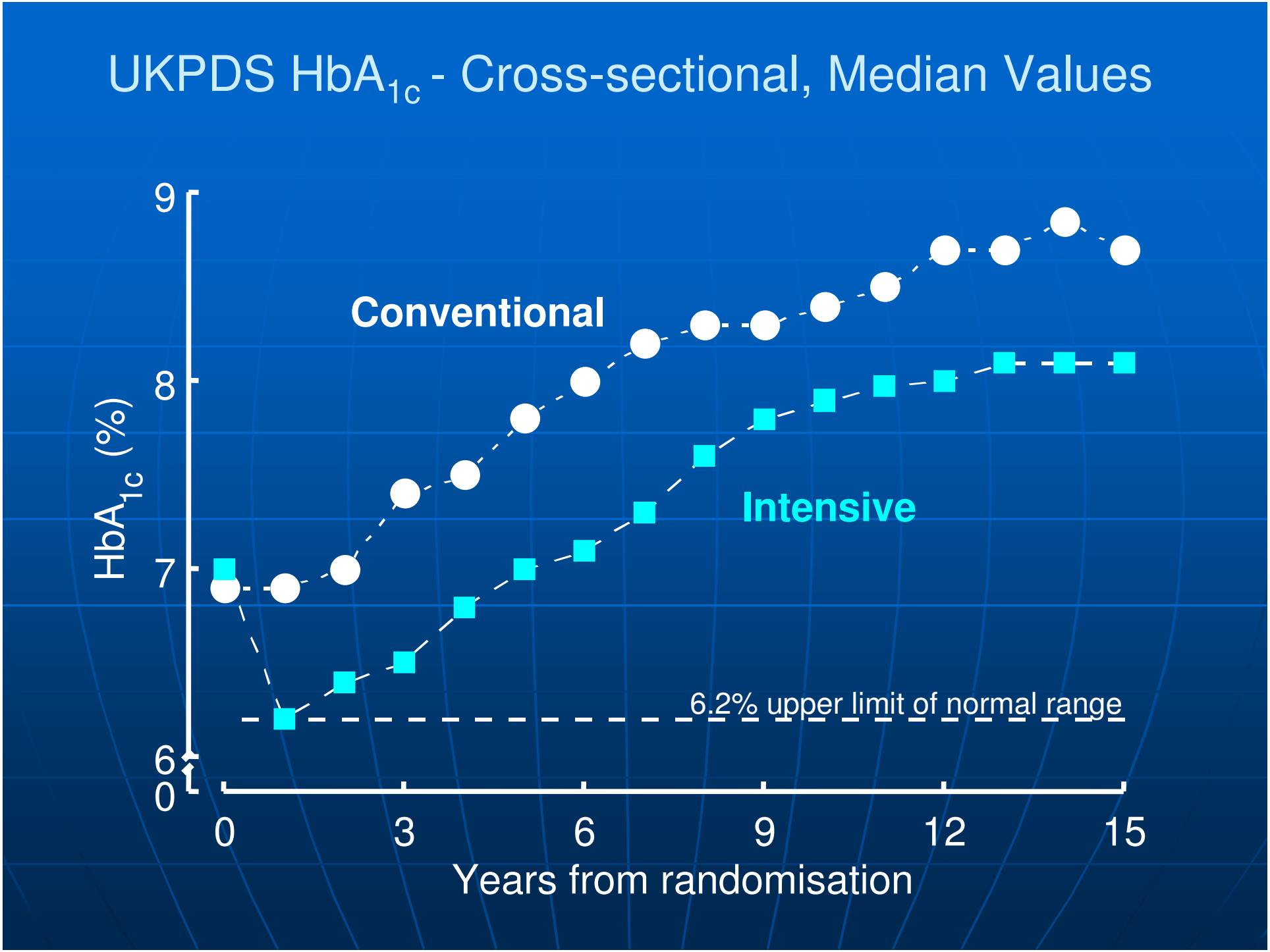
UKPDS Group. *Lancet* 1998; **352**: 854–865.

Proportion of overweight people with Type 2 diabetes treated with metformin maintaining target HbA_{1c} (< 7%)

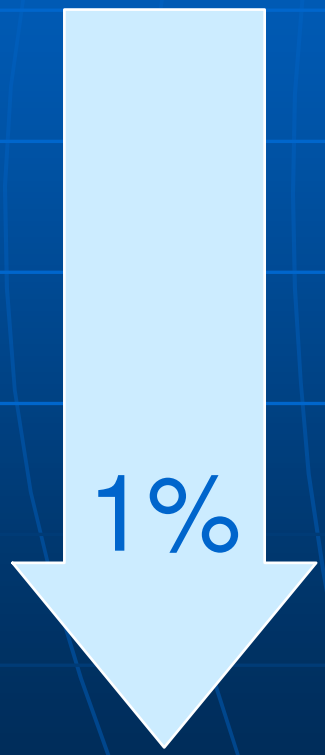


Turner RC *et al. JAMA* 1999; **281**: 2005–2012.

UKPDS HbA_{1c} - Cross-sectional, Median Values



Lessons from UKPDS: Better Control Means Fewer Complications



	REDUCED RISK*
Deaths from diabetes	–21%
Heart attacks	–14%
Microvascular complications	–37%
Peripheral vascular disorders	–43%

UKPDS 35. BMJ 2000;321:405–12

*p<0.0001

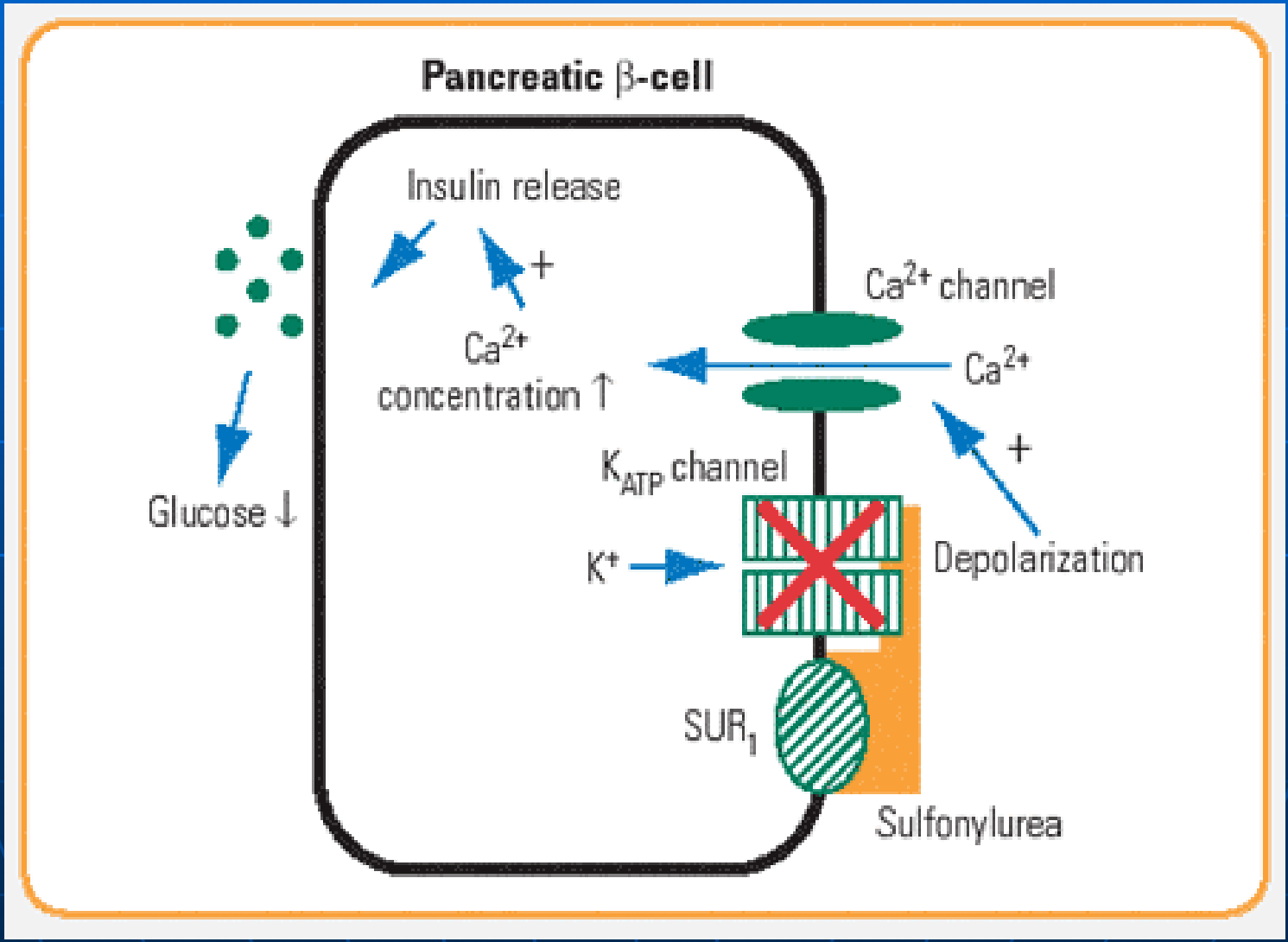
Hypoglycaemic Agents

- α glucosidase inhibitors
- Metaglinides
- Metformin
- Sulphonylureas
- Thiazolidindiones
- GLP – 1 analogues
- DPP IV inhibitors
- SGLT2 inhibitors

Sulphonylureas

- Have been around since the 1950's
- Act by binding to the SU receptor causing an influx of Ca^{2+} and an exocytosis of insulin containing vesicles
- Relies on adequate β cell function
- Good for rapid symptom relief

Sulphonylureas



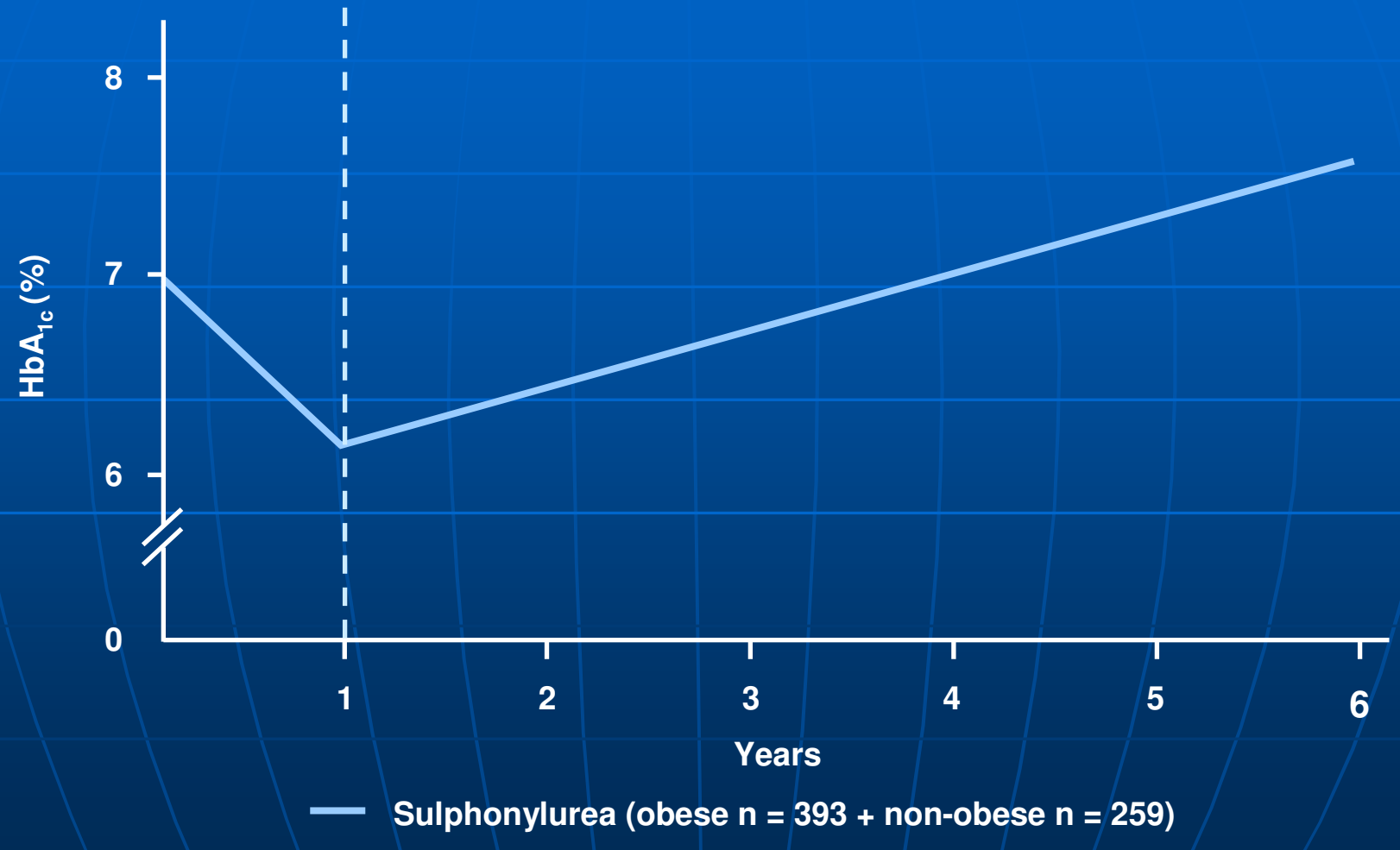
Sulphonylureas

- Use limited to individuals with a BMI < 25 or in whom metformin is contraindicated
- When used in combination, they flatten glucose excursions
- Can be used in combination with most other oral hypoglycaemic agents

Sulphonylureas

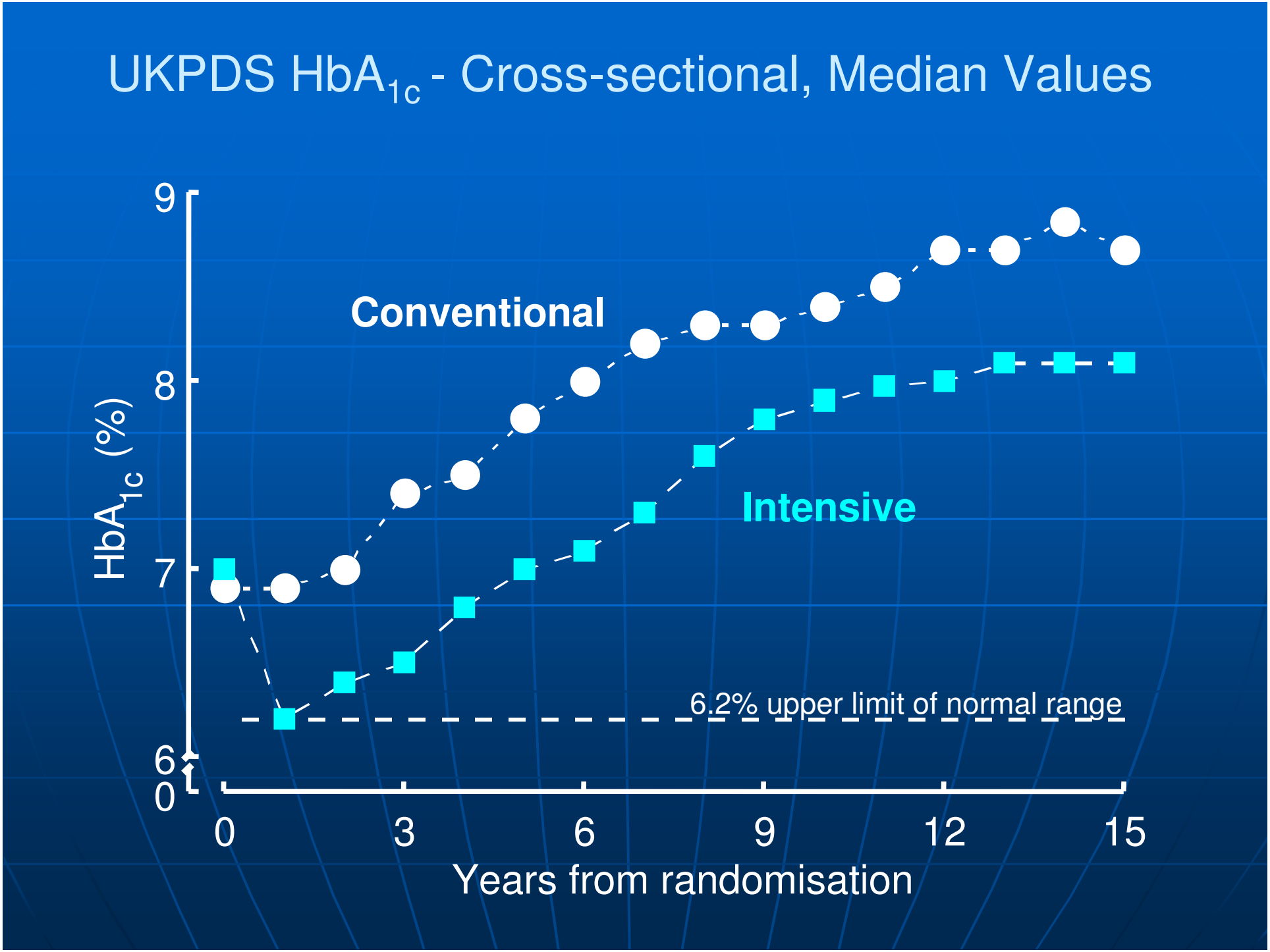
- Their long half life makes hypoglycaemia more likely, especially in the elderly
- Avoid in hepatic or renal failure
- Maximum HbA_1C reduction is 1.5%
- Weight gain is common

Glycaemic Control Starts to Deteriorate After 1 Year with a Sulphonylurea

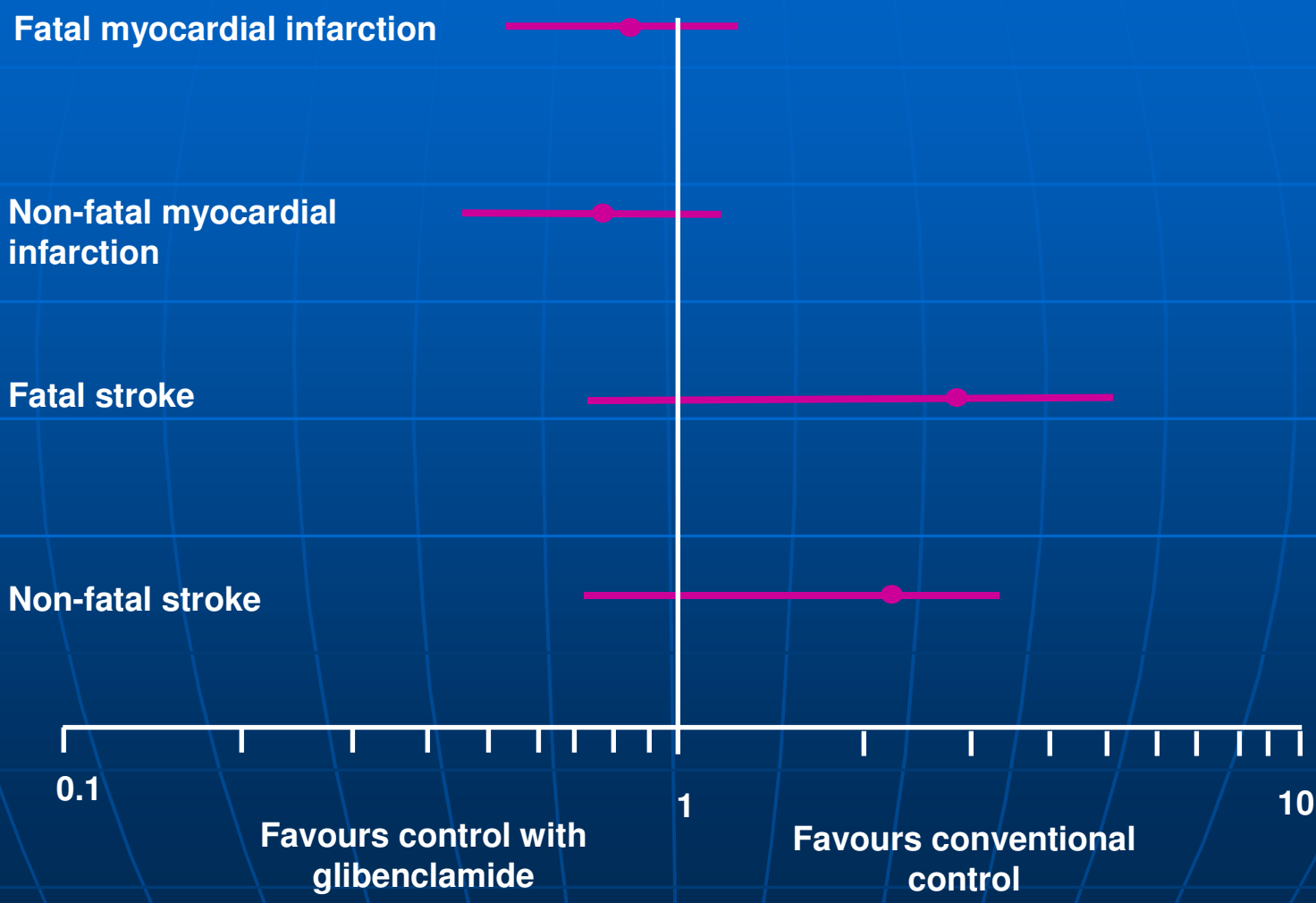


UKPDS Group. *Diabetes* 1995; **44**: 1249–1258.

UKPDS HbA_{1c} - Cross-sectional, Median Values



UKPDS: Sulphonylureas Have No Impact on Cardiovascular Outcomes



UKPDS Group. *Lancet* 1998; **352**: 837–853.

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- DPP IV inhibitors
- SGLT2 inhibitors

Thiazolidinediones

- Pioglitazone (rosiglitazone was withdrawn in 2010)
- Work by increasing peripheral insulin sensitivity at a nuclear level on peroxisome proliferator-activated receptor γ (PPAR γ)
- "First do no harm"

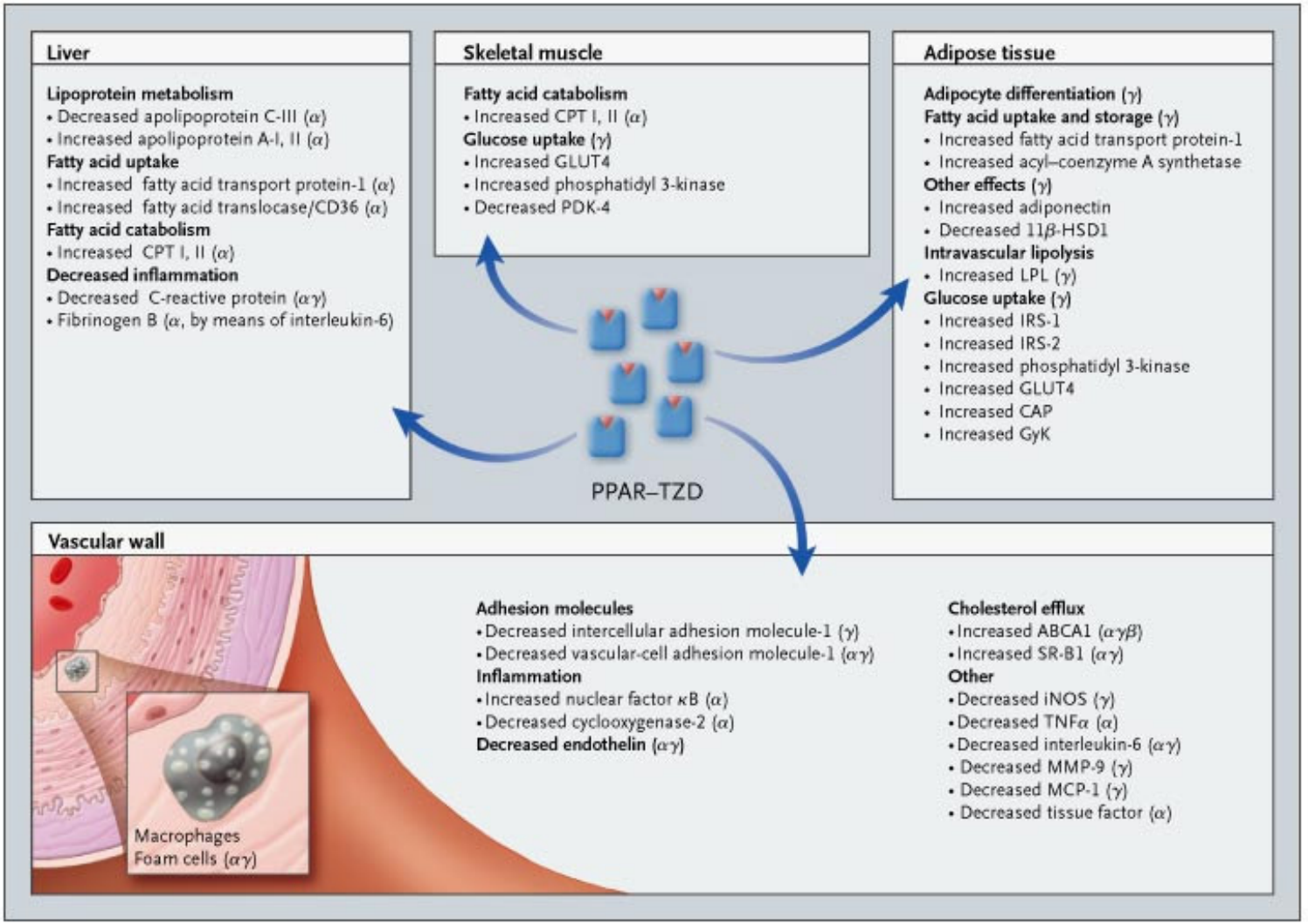
Thiazolidinediones

- Maximum HbA_1C reduction is 1.5%
- But this takes 4 to 6 months to achieve maximal benefit so give it time!
- Potential other benefits when considering type 2 diabetes as an 'endotheliopathy' outweighed by other factors

Thiazolidinediones

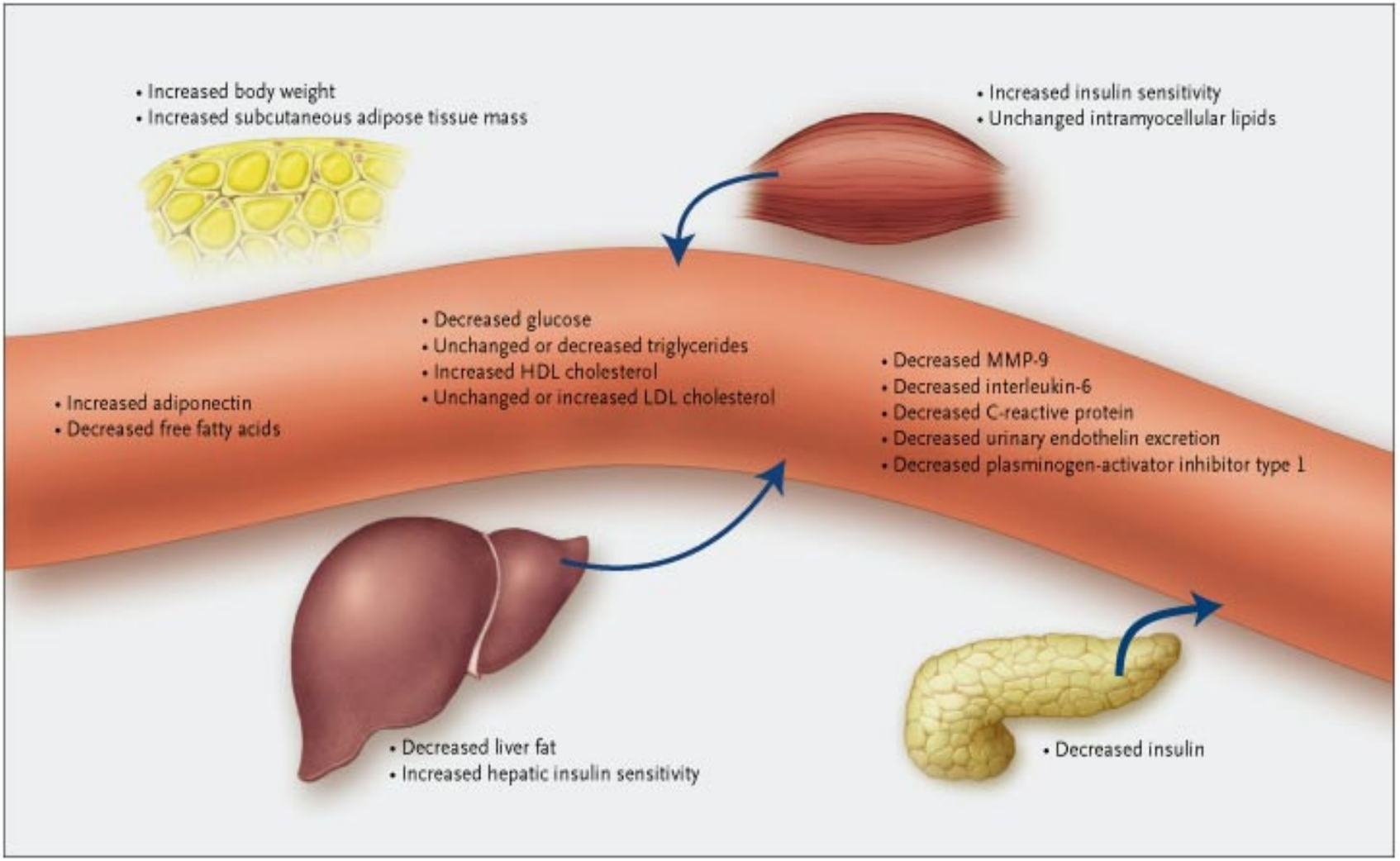
- Work by altering gene expression
- PPAR α and δ also important as receptors for fatty acids and their metabolites and thus play a role the regulation of glucose, fatty acid, and cholesterol metabolism
- Combination PPAR $\alpha\gamma$ agents were withdrawn due to safety concerns

TZD's – Molecular Targets



Yki-Jarvinen, H. N Engl J Med 2004;351:1106-1118

Mechanism of Action of Thiazolidinediones in Vivo in Humans



Yki-Jarvinen, H. N Engl J Med 2004;351:1106-1118

Comparative Effects of Maximal Doses of Rosiglitazone (8 mg) and Pioglitazone (30 to 45 mg) on Glycaemic Control as Measured by Absolute Change in Glycosylated Haemoglobin as Compared with Placebo or Control Group (Metformin, Sulphonylurea, or Insulin Alone or in Combination)

Type of Therapy	Study	No. of Patients	Duration of Study	Decrease in Glycosylated Hemoglobin	Weight Gain*
			wk	%	*kg*
Pioglitazone					
Monotherapy	Aronoff et al.[17]	155	26	1.6	4.1
	Scherbaum and Göke[18]	162	26	0.7	1.9
	Rosenblatt et al.[19]	197	23	1.4	3.2
Combination therapy					
Metformin	Einhorn et al.[20]	328	16	0.8	2.3
Sulfonylurea	Kipnes et al.[21]	376	16	1.3	3.7
Insulin	Rosenstock et al.[22]	358	16	1.0	3.7
Rosiglitazone					
Monotherapy	Lebovitz et al.[23]	327	26	1.5	4.5
Combination therapy					
Metformin	Fonseca et al.[24]	223	26	1.2	3.1
	Gomez-Perez et al.[25]	70	26	1.5	3.3
Sulfonylurea	Vongthavaravat et al.[26]	348	26	1.2	—
Insulin	Raskin et al.[27]	207	26	1.3	4.4

* A dash indicates no data.

Yki-Jarvinen, H. N Engl J Med 2004;351:1106-1118

Thiazolidinediones

- Combination tablet with metformin or glimeparide now available
- Licensed for triple therapy

Thiazolidinediones

- Need to check LFT's periodically
- Avoid in hepatic impairment
- Avoid in CCF (fluid retention)
- Fracture risk vastly increased – avoid in women
- Early data to show that they cause macular oedema

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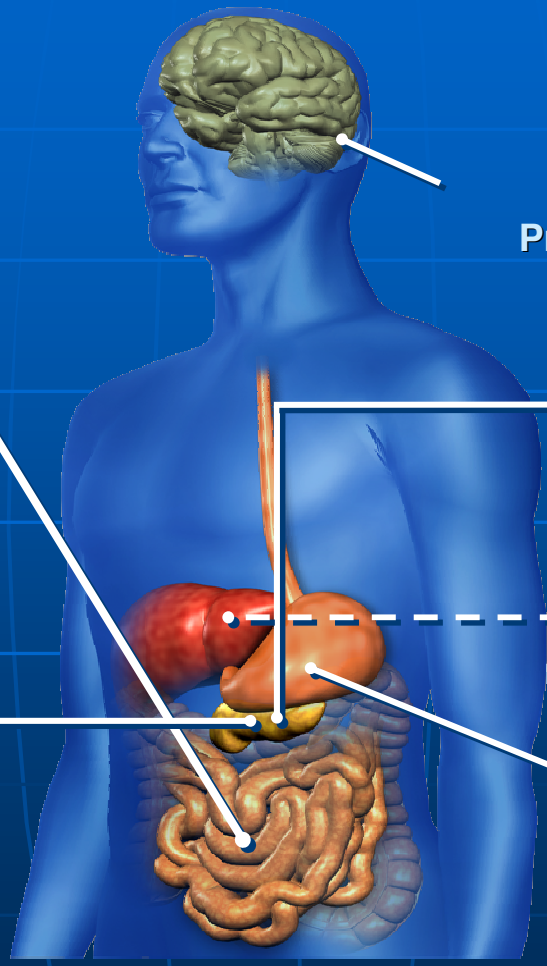
GLP-1 Analogues

- Exentatide and Liragultide

GLP-1 and DPP-IV



GLP-1 secreted upon the ingestion of food

5.Brain:
Promotes satiety and reduces appetite

2.α-cell:
Suppresses postprandial glucagon secretion

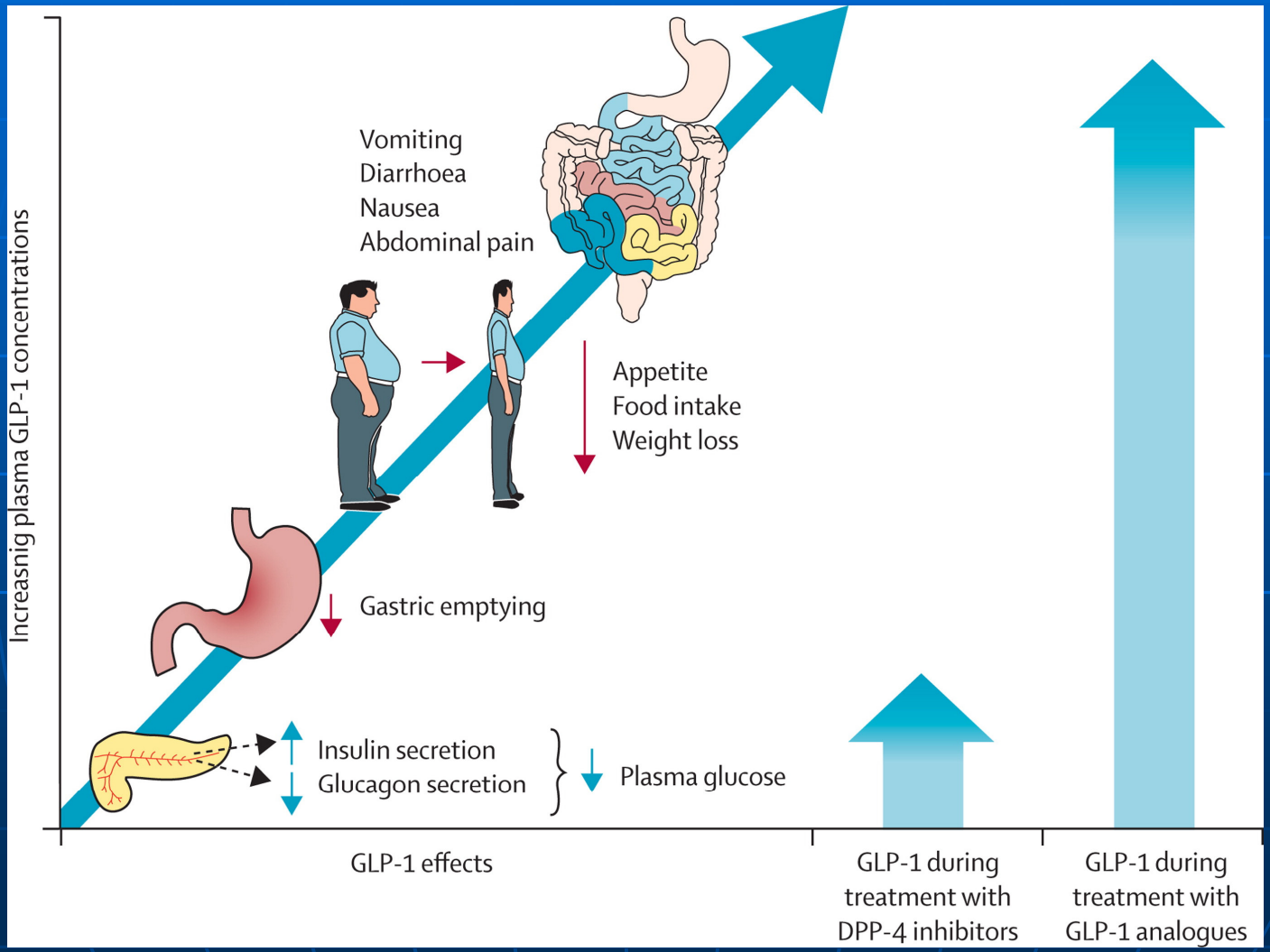
3.Liver:
reduces hepatic glucose output

1.β-cell:
Enhances glucose-dependent insulin secretion in the pancreas

4.Stomach:
slows the rate of gastric emptying

Nauck MA et al. *Diabetologia* 1993;36:741–744; Larsson H et al. *Acta Physiol Scand* 1997;160:413–422; Nauck MA et al. *Diabetologia* 1996;39:1546–1553; Flint A et al. *J Clin Invest* 1998;101:515–520; Zander et al. *Lancet* 2002;359:824–830.

Different Effects at Different Doses



Madsbad S Lancet 2009;373(9662):439-439

Do They Work?

- HbA_1C reduction of about 1.1%
- Extensive weight loss
- ? B cell preservation
- 5mg bd $^{s}/_{c}$ fixed dose
- Expensive
- Haemorrhagic pancreatitis

Hypoglycaemic Agents

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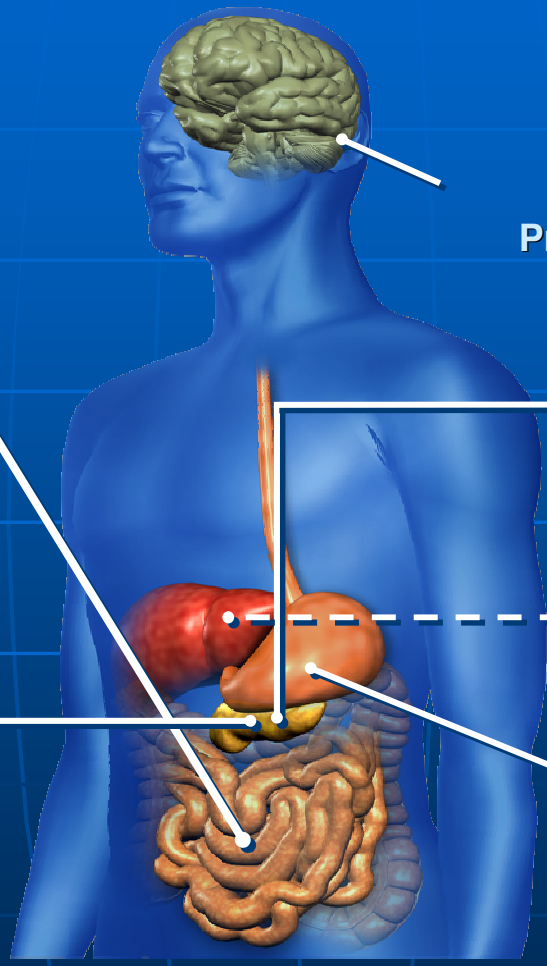
DPP-IV Antagonists

- Sitagliptin and Vildagliptin

GLP-1 and DPP-IV



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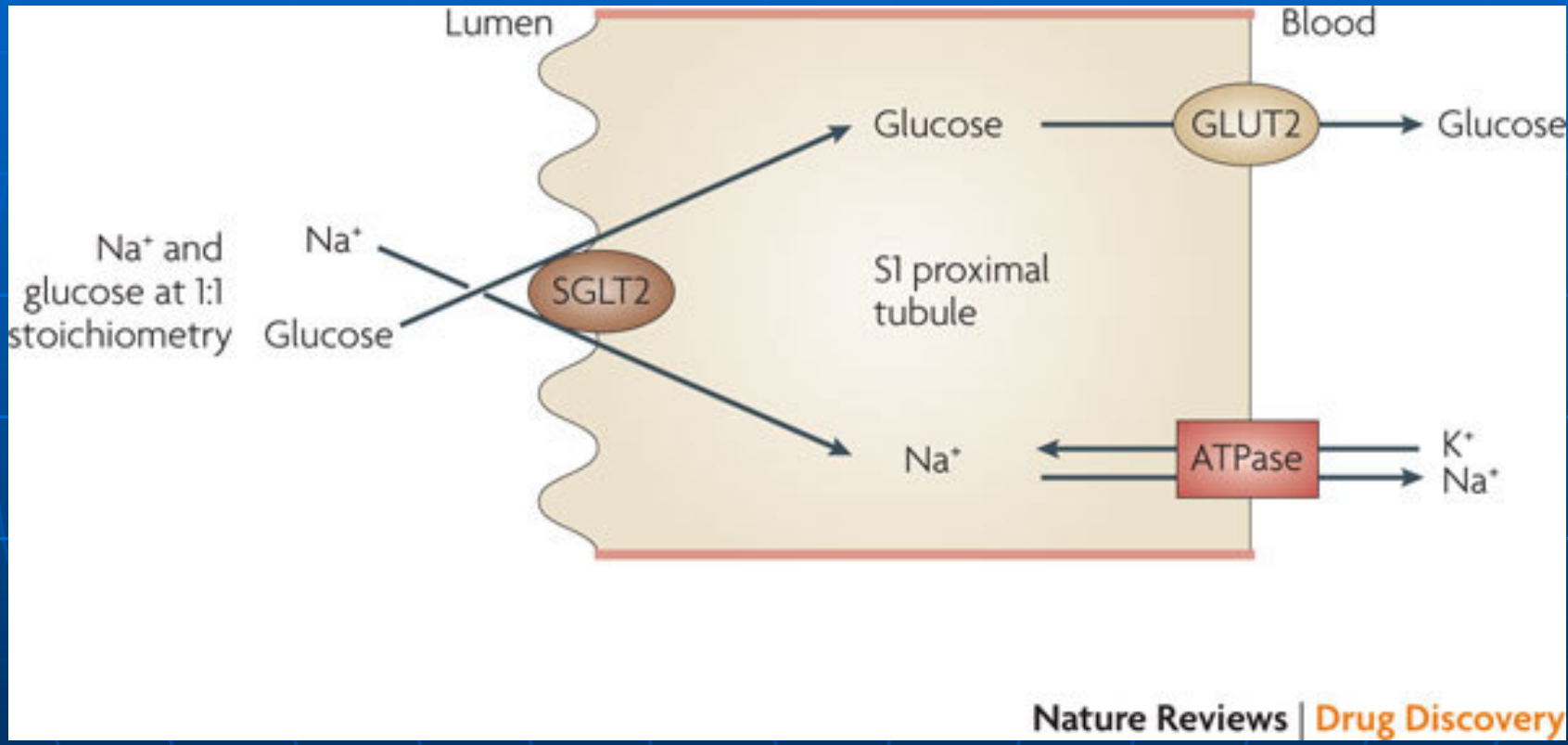
SGLT2 Inhibitors



Chao EC Nature Rev Drug Disc 2010;9(7):551-559

SGLT2 Inhibitors

- Work independently of insulin to inhibit glucose re-uptake from the proximal convoluted renal tubule
- Can be used in type 1 or type 2 diabetes
- Can be used in combination with any other agent

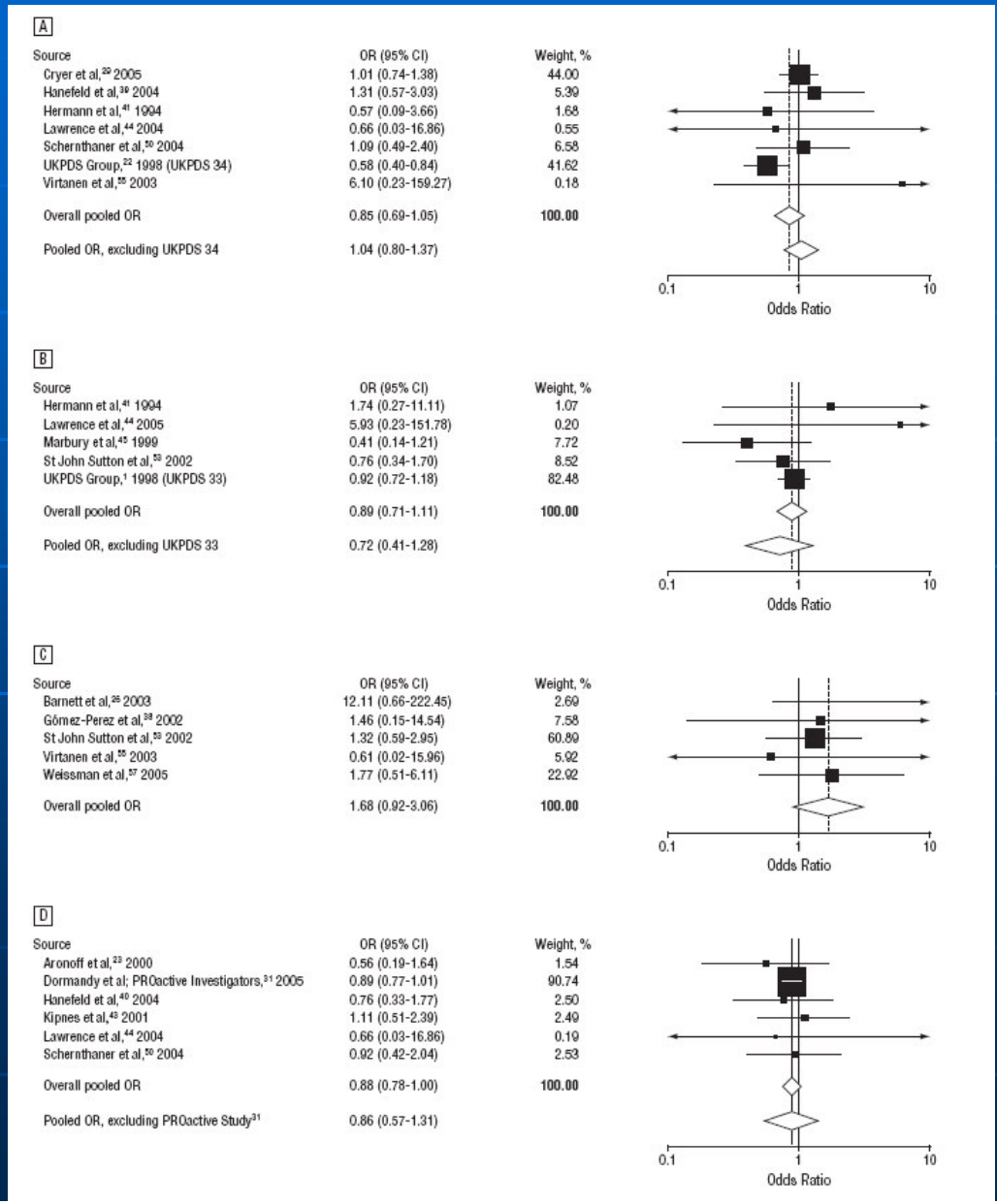
SGLT2 Inhibitors

- Developed from the bark of the apple tree
- Hba1c reduction ~ 6mmol/mol (0.75%)
- Associated with weight loss

SGLT2 Inhibitors

- Safety
  - No increased incidence of hypos
  - No increased incidence of UTI's
  - Increase in urinary volumes by 4-600mls/day
  - Slight increase in thrush

Safety Issues



A

Source	OR (95% CI)	Weight, %
Cryer et al,[39] 2005	1.01 (0.74-1.38)	44.00
Hanefeld et al,[39] 2004	1.31 (0.57-3.03)	5.39
Hermann et al,[41] 1994	0.57 (0.09-3.66)	1.68
Lawrence et al,[44] 2004	0.66 (0.03-16.86)	0.55
Schernthaner et al,[50] 2004	1.09 (0.49-2.40)	6.58
UKPDS Group,[22] 1998 (UKPDS 34)	0.58 (0.40-0.84)	41.62
Virtanen et al,[55] 2003	6.10 (0.23-159.27)	0.18
Overall pooled OR	0.85 (0.69-1.05)	**100.00**
Pooled OR, excluding UKPDS 34	1.04 (0.80-1.37)	

B

Source	OR (95% CI)	Weight, %
Hermann et al,[41] 1994	1.74 (0.27-11.11)	1.07
Lawrence et al,[44] 2005	5.93 (0.23-151.78)	0.20
Marbury et al,[45] 1999	0.41 (0.14-1.21)	7.72
St John Sutton et al,[55] 2002	0.76 (0.34-1.70)	8.52
UKPDS Group,[1] 1998 (UKPDS 33)	0.92 (0.72-1.18)	82.48
Overall pooled OR	0.89 (0.71-1.11)	**100.00**
Pooled OR, excluding UKPDS 33	0.72 (0.41-1.28)	

C

Source	OR (95% CI)	Weight, %
Barnett et al,[26] 2003	12.11 (0.66-222.45)	2.69
Gómez-Perez et al,[38] 2002	1.46 (0.15-14.54)	7.58
St John Sutton et al,[55] 2002	1.32 (0.59-2.95)	60.89
Virtanen et al,[55] 2003	0.61 (0.02-15.96)	5.92
Weissman et al,[57] 2005	1.77 (0.51-6.11)	22.92
Overall pooled OR	1.68 (0.92-3.06)	**100.00**

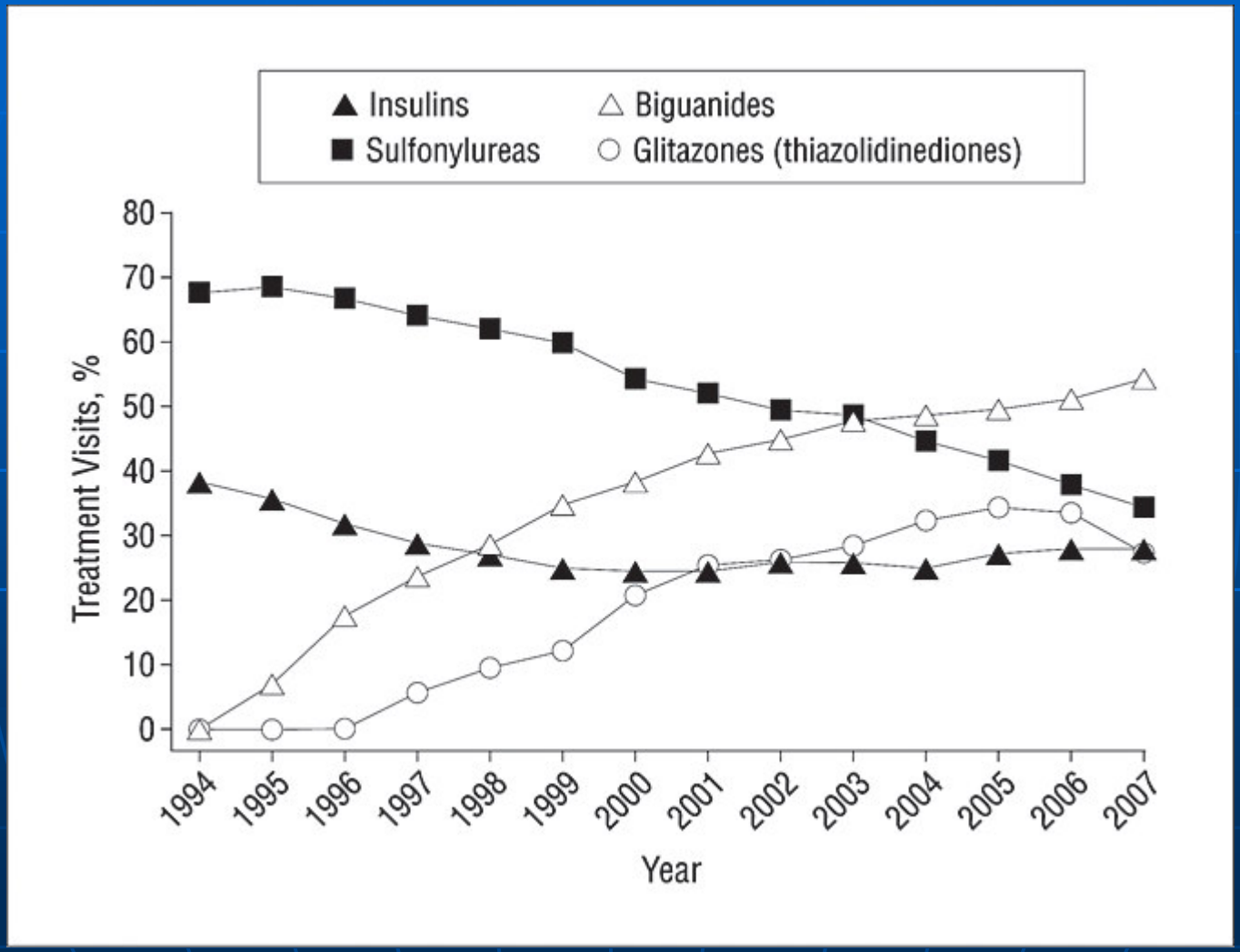
D

Source	OR (95% CI)	Weight, %
Aronoff et al,[23] 2000	0.56 (0.19-1.64)	1.54
Dormandy et al; PROactive Investigators,[31] 2005	0.89 (0.77-1.01)	90.74
Hanefeld et al,[40] 2004	0.76 (0.33-1.77)	2.50
Kipnes et al,[43] 2001	1.11 (0.51-2.39)	2.49
Lawrence et al,[44] 2004	0.66 (0.03-16.86)	0.19
Schernthaner et al,[50] 2004	0.92 (0.42-2.04)	2.53
Overall pooled OR	0.88 (0.78-1.00)	**100.00**
Pooled OR, excluding PROactive Study[31]	0.86 (0.57-1.31)	

- Metformin is the safest
- SU's are neutral
- Rosi is bad
- Pio is OK

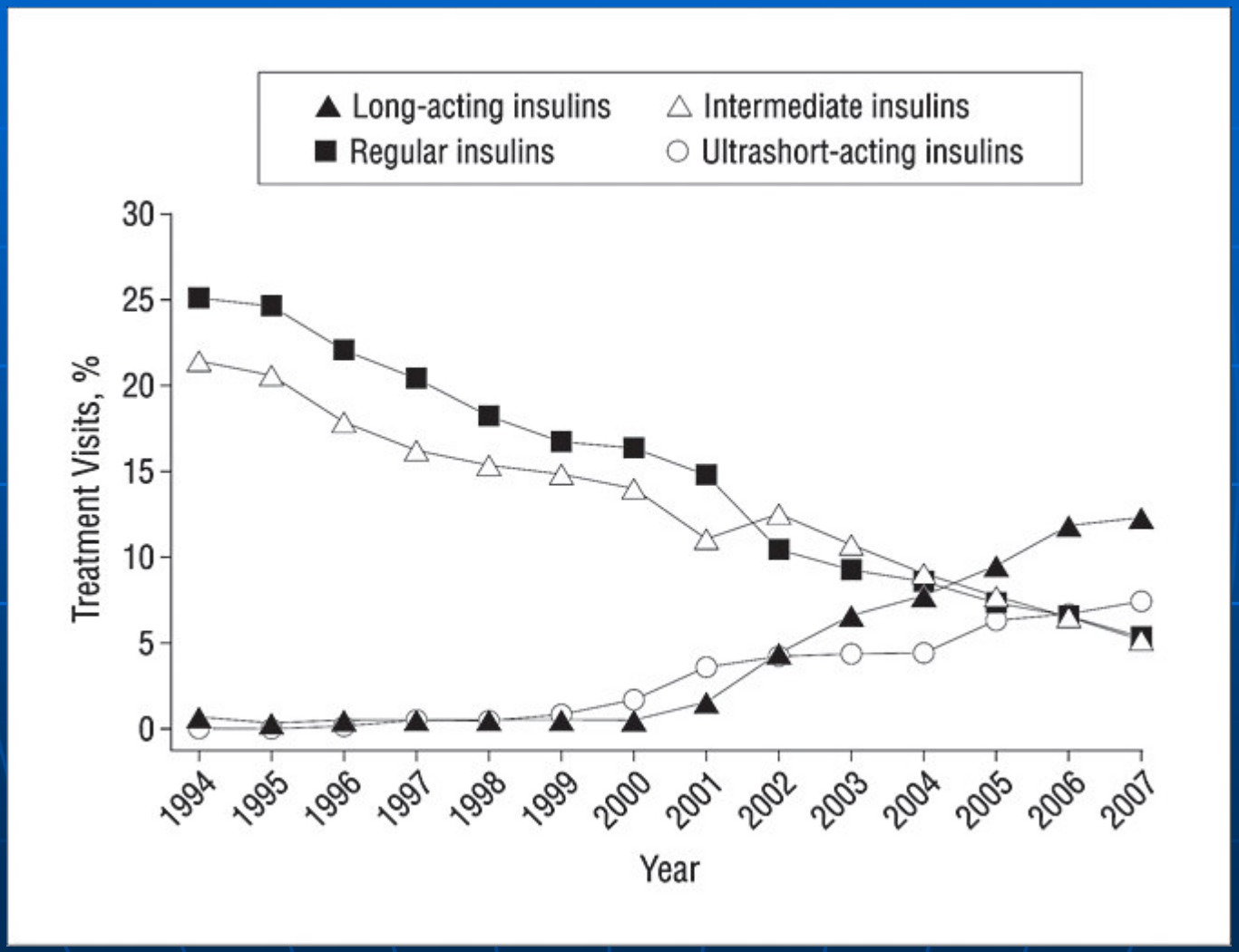
Selvin E et al Arch Int Med 2008;186(19):2070-2080

US Trends in OHA Use



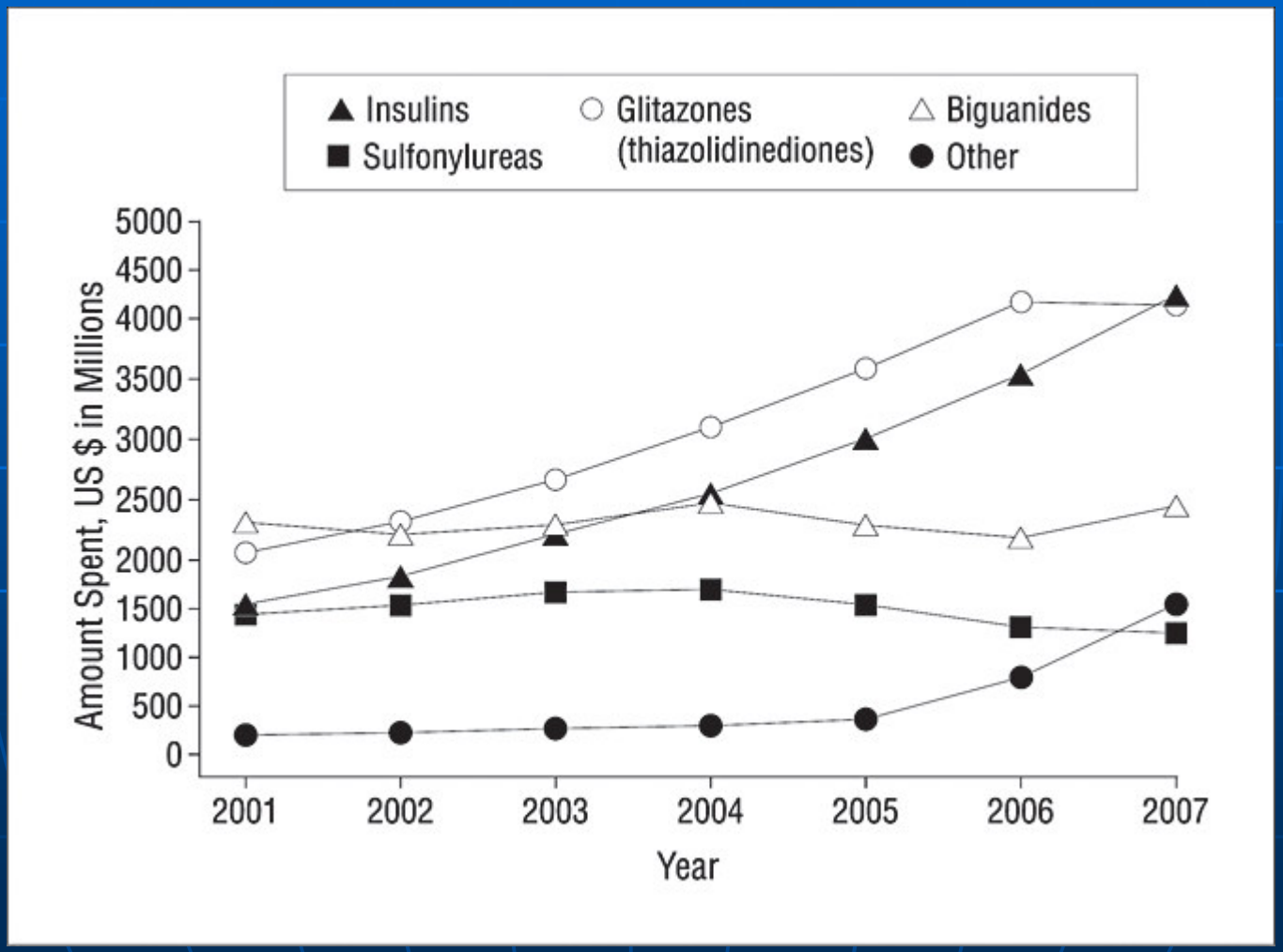
Alexander et al Arch Int Med 2008;168(19):2088-2094

US Trends in Insulin Use



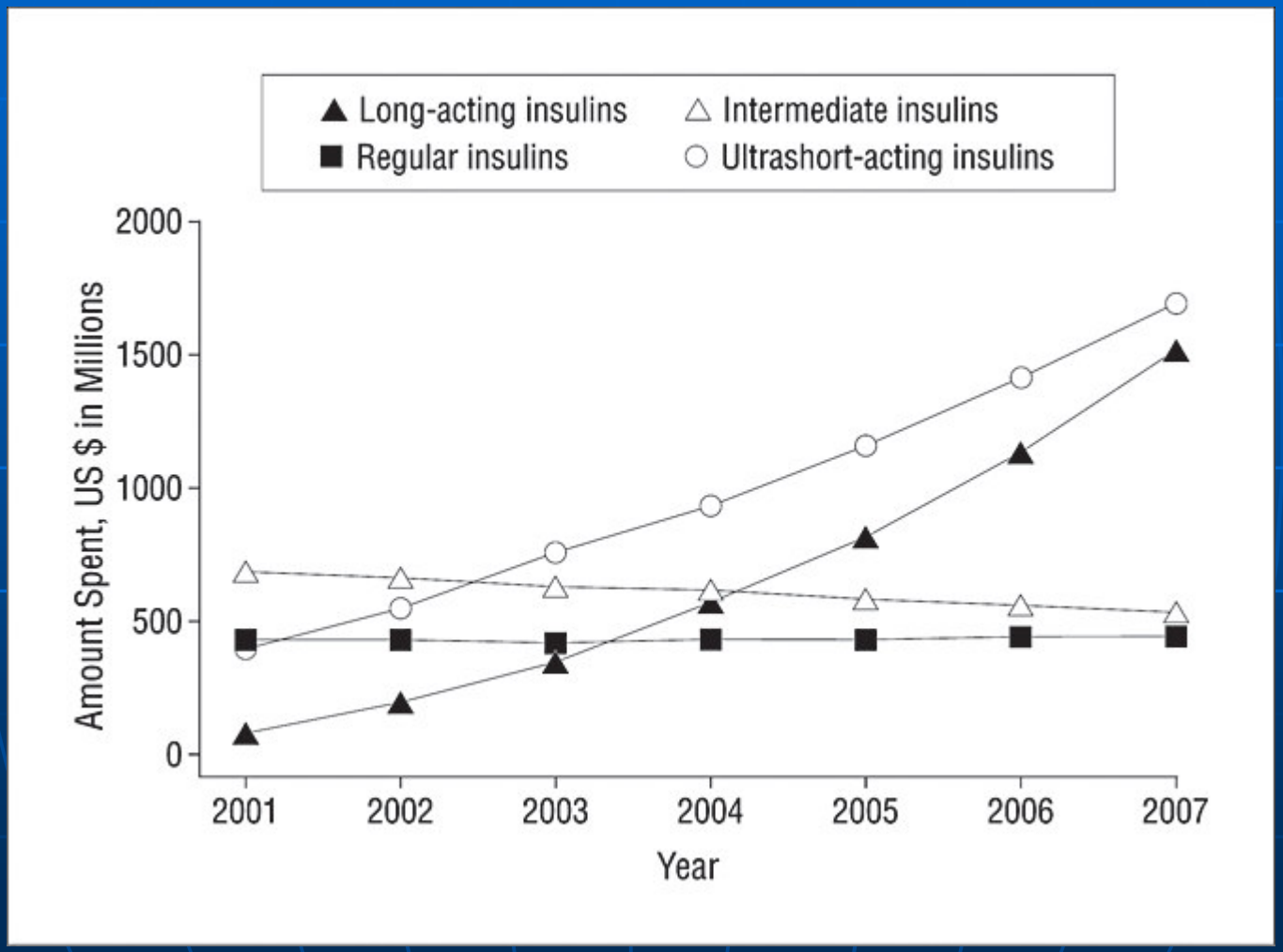
Alexander et al Arch Int Med 2008;168(19):2088-2094

Increased Costs - Overall



Alexander et al Arch Int Med 2008;168(19):2088-2094

Increased Insulin Costs



Alexander et al Arch Int Med 2008;168(19):2088-2094

Things That Make the Most Difference

- Smoking OR 2.87
- Raised ApoB/ApoA1 ratio OR 3.25
- History of hypertension OR 1.91
- Diabetes OR 2.37
- Abdominal obesity OR 1.12
- Psychosocial factors OR 2.67
- Daily fruit and veg intake OR 0.7
- Regular alcohol consumption OR 0.9
- Regular physical activity OR 0.86

Yusuf et al Lancet 2004 364:937-952

Metabolic Syndrome – ATP III

Abdominal obesity, given as waist circumference*	
Men	>102 cm (>40 in)
Women	>88 cm (>35 in)
Triglycerides	3.87 mmol/l
HDL cholesterol	
Men	<1.0 mmol/l
Women	<1.3 mmol/l
Blood pressure	130/ 85 mm Hg
Fasting glucose	6.0 mmol/l

Circulation. 2002; 106: 3143–3421

Metabolic Syndrome – WHO

Insulin resistance, identified by 1 of the following:
• Type 2 diabetes
• Impaired fasting glucose
• Impaired glucose tolerance
• or for those with normal fasting glucose levels (<110 mg/dL, 5.94 mmol/l), glucose uptake below the lowest quartile for background population under investigation under hyperinsulinemic, euglycemic conditions
Plus any 2 of the following:
• Antihypertensive medication and/or high blood pressure (140 mm Hg systolic or 90 mm Hg diastolic)
• Plasma triglycerides 150 mg/dL (1.7 mmol/L)
• HDL cholesterol <35 mg/dL (<0.9 mmol/L) in men or <39 mg/dL (1.0 mmol/L) in women
• BMI >30 kg/m^2 and/or waist:hip ratio >0.9 in men, >0.85 in women
• Urinary albumin excretion rate 20 µg/min or albumin:creatinine ratio 30 mg/g

http://whqlibdoc.who.int/hq/1999/WHO_NCD_NCS_99.2.pdf.

Metabolic Syndrome – IDF

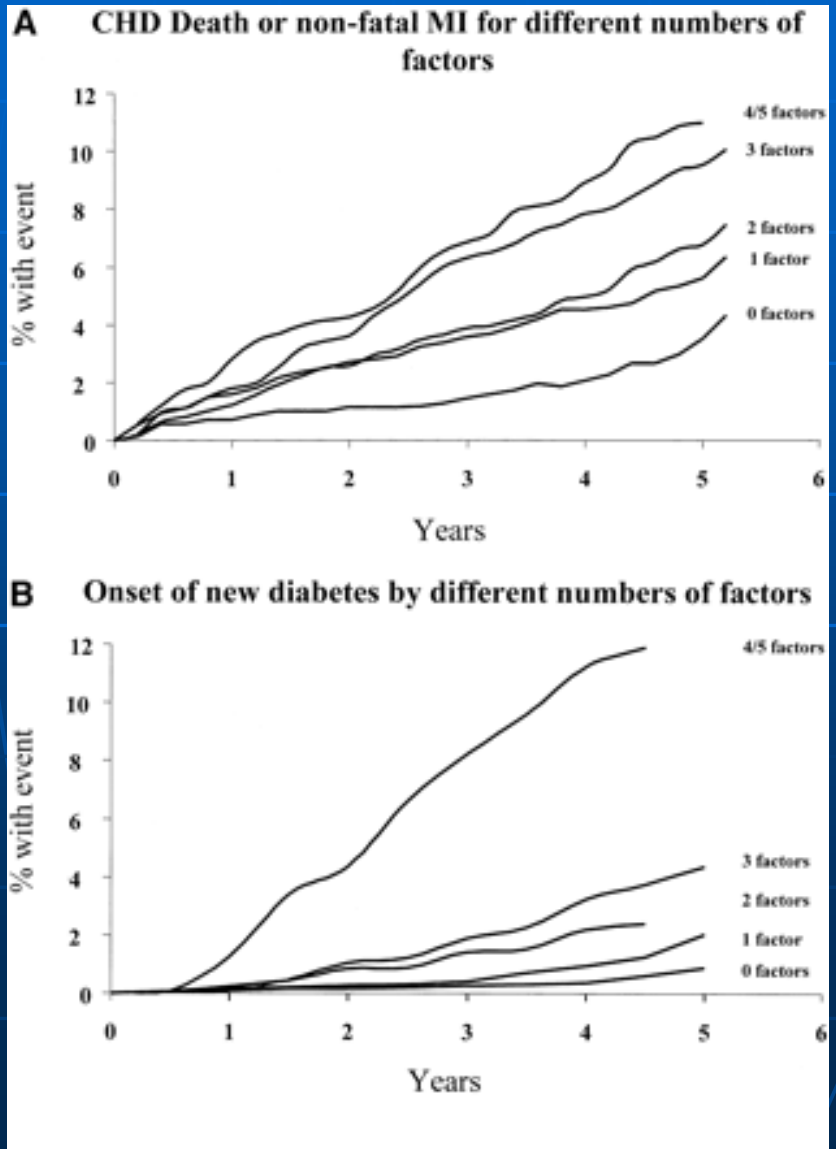
- Central Obesity
  - Defined as waist circumference ≥ 94cm for Europid men and ≥ 80 cm for Europid women
- Plus ANY TWO of the following four factors
  - Raised TG: ≥ 1.7mmol/l **or if specificly treated**
  - Low HDL: < 1.03mmol/l in men or < 1.29 in women **or if specificly treated**
  - Raised BP: Systolic ≥ 130 or diastolic ≥ 85 **or treatment of previously diagnosed hypertension**
  - Raised fasting plasma glucose ≥ 5.6mmol/l **or previously diagnosed type 2 diabetes**. (If > 5.6 OGTT strongly recommended)

http://www.idf.org/webdata/docs/IDF_Metasyndrome_definition.pdf Accessed 10/5/05

Agreement?

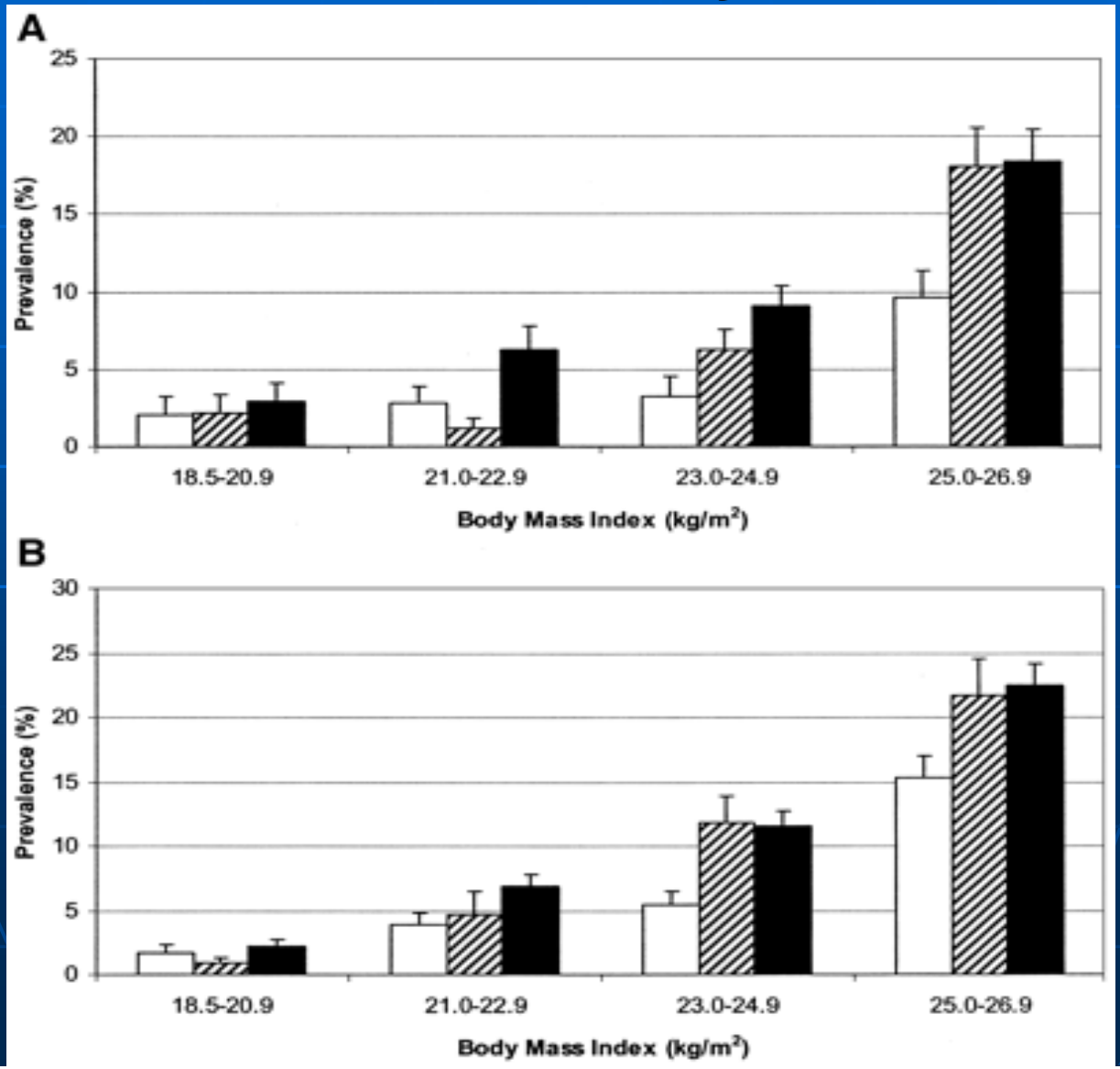
- Anywhere between 35 and 75% depending on what definitions you compare
- However, CV risk is increased depending on how many components of the metabolic syndrome are present

CVD Event Rate vs Number of Risk Factors (Metabolic Syndrome)



Sattar et al Circulation 2003;108:414-419

BMI is Directly Related to Risk of Development of the Metabolic Syndrome



A = Men

B = Women

= Blacks

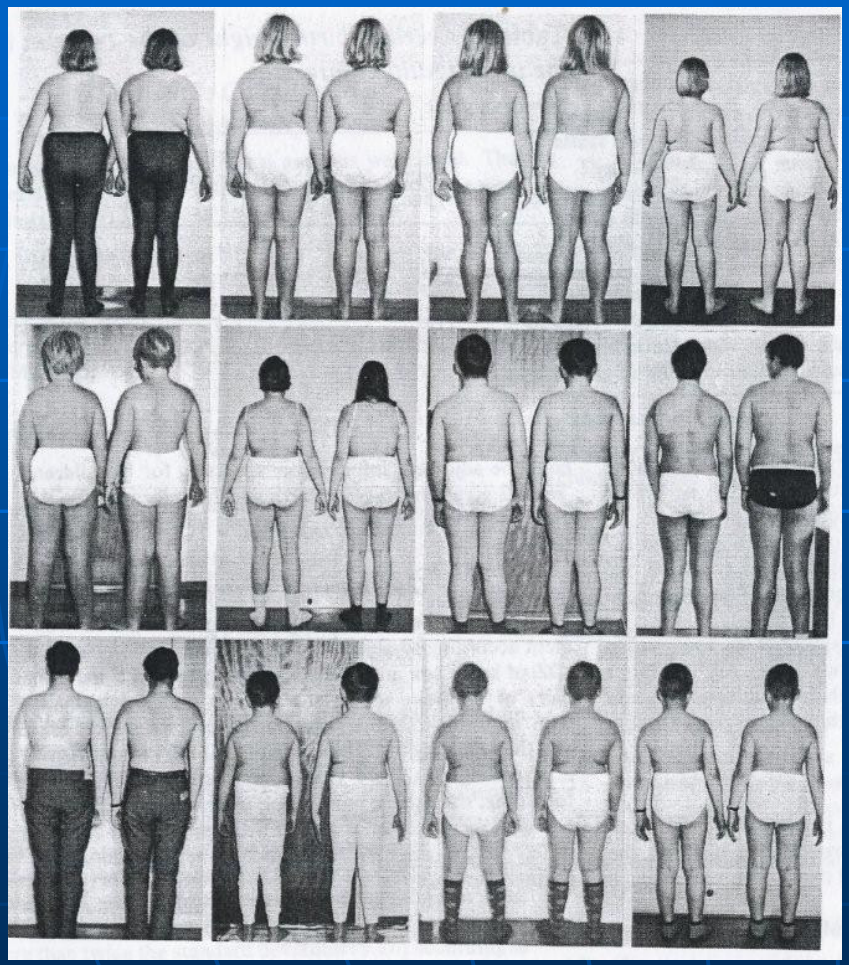
= Hispanics

= Whites

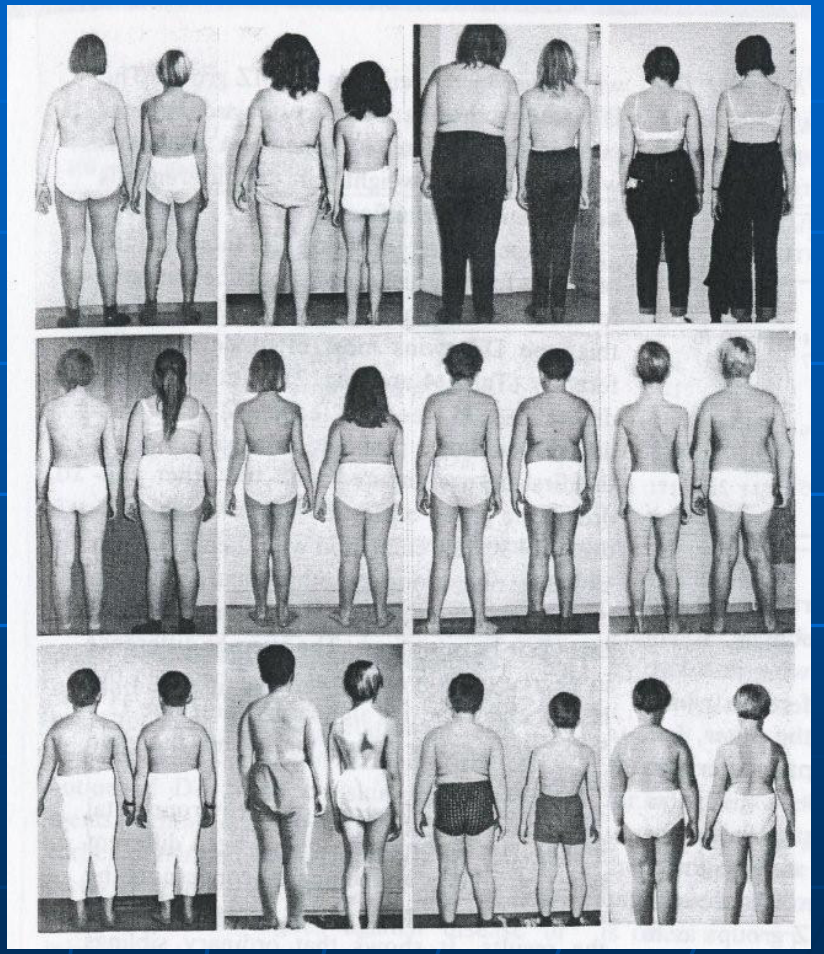
St Onge MP et al Diabetes Care 2004;27(9):2222-2228

Time Magazine 23rd June 2008

Is it All in The Genes?



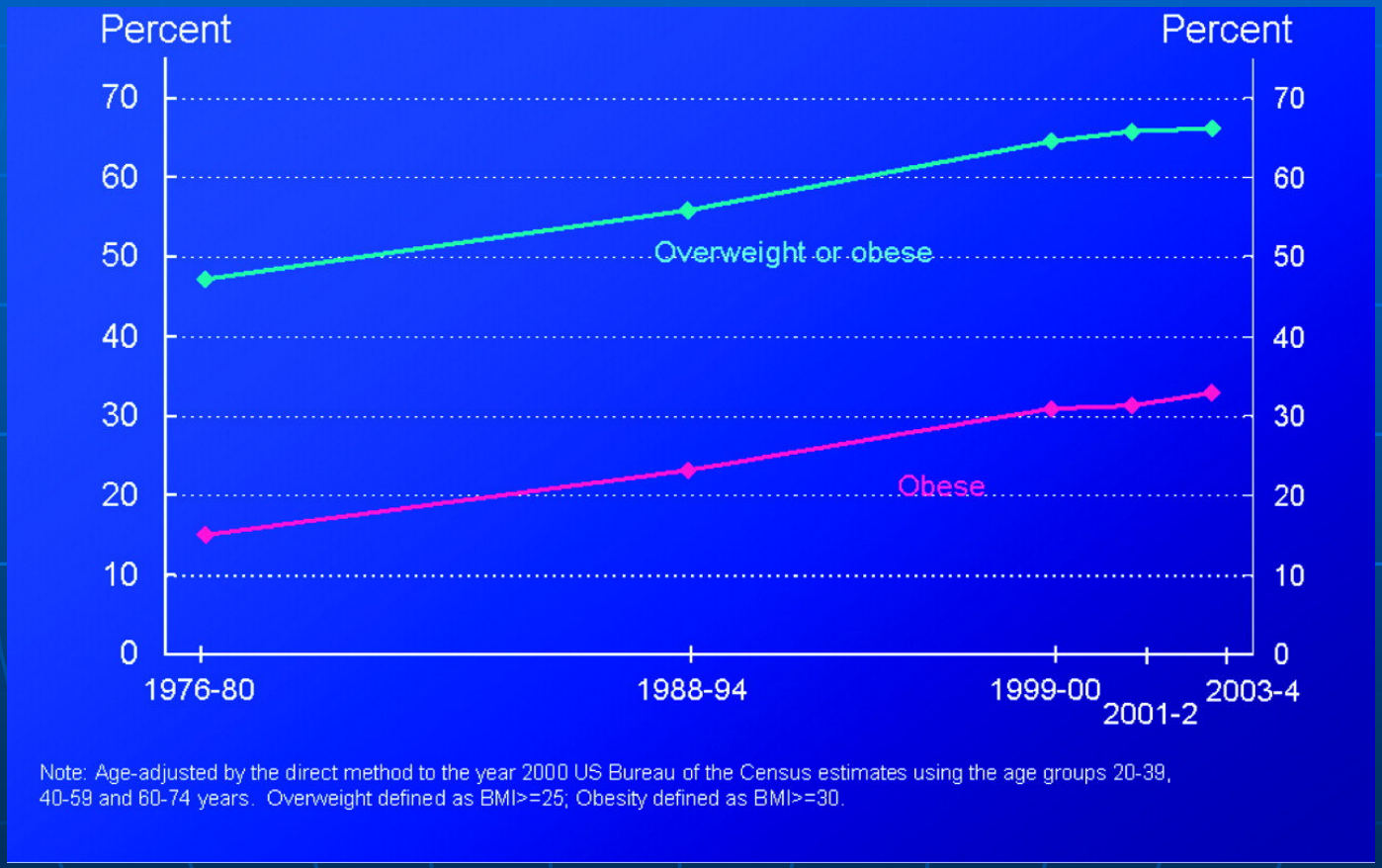
Monozygotic Twins



Dizygotic Twins

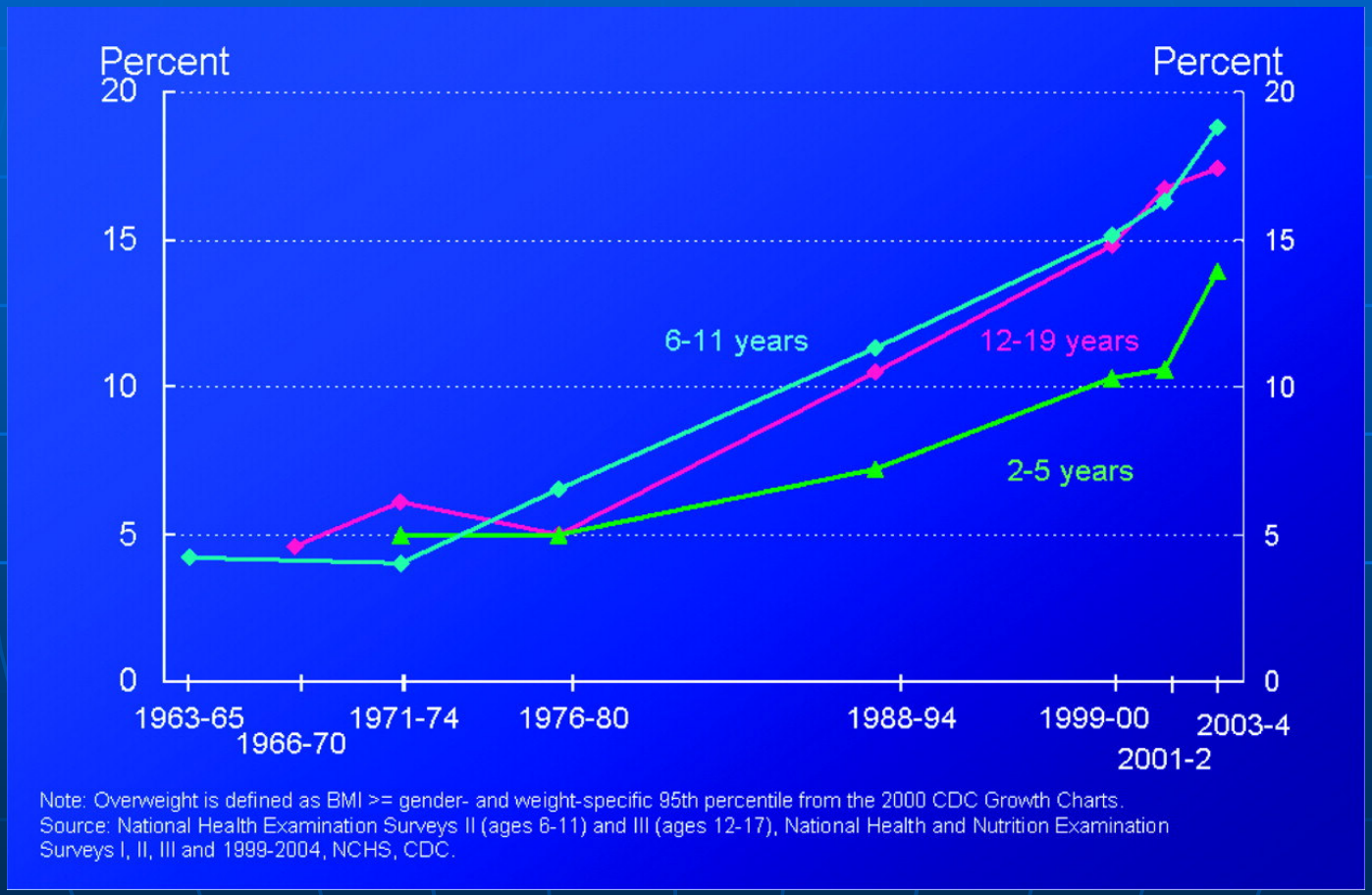
Borjeson M Acta Paed Scand 1976;65:279-287

Trends in US Adult Overweight and Obesity - 20 to 74 Years



Kumanyika et al. Circulation 2008;118:428-464

Trends in US Childhood Overweight



Kumanyika et al. Circulation 2008;118:428-464

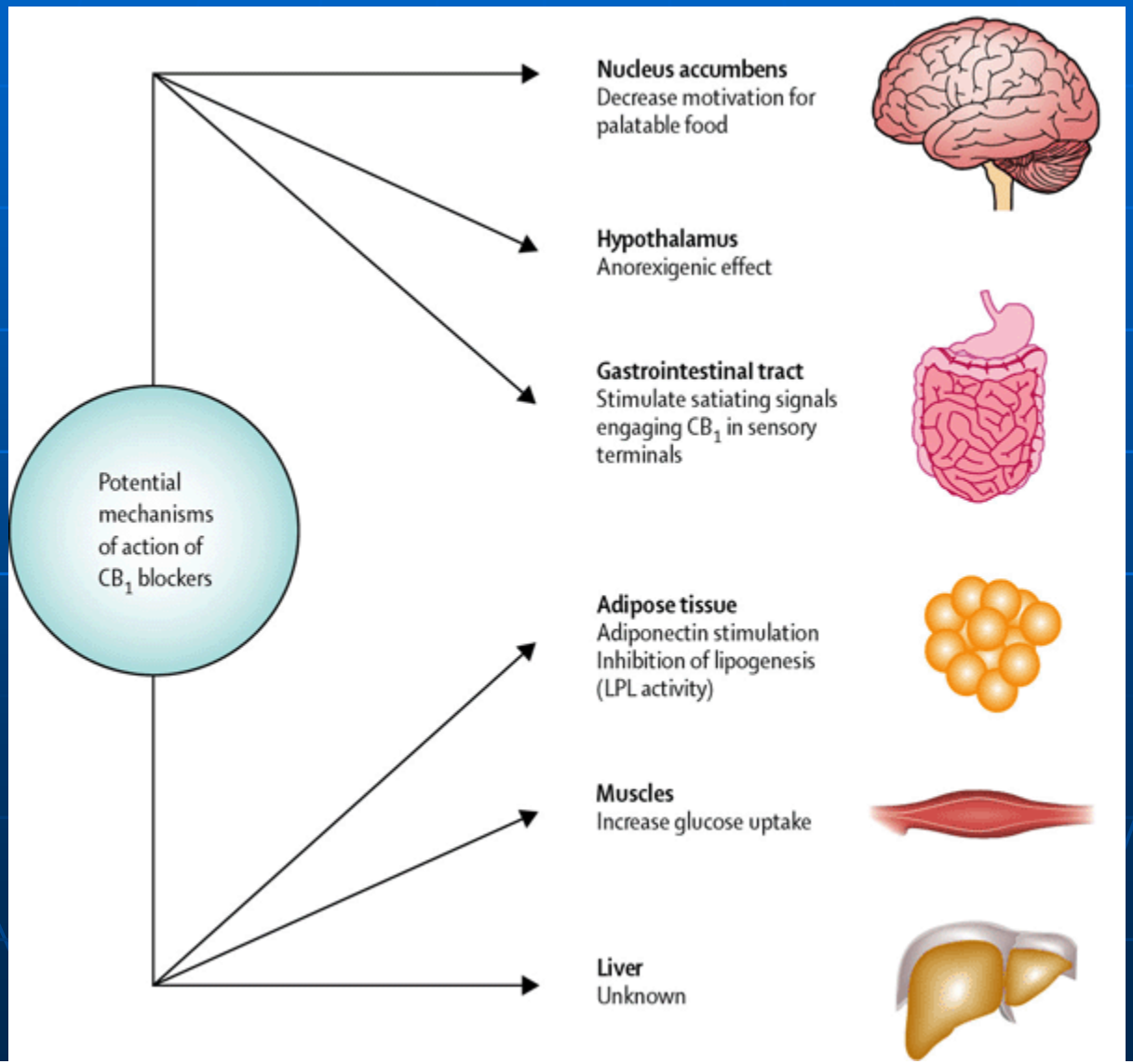
2 Drugs available

- Orlistat
- Sibutramine

Rimonabant (Acomplia)

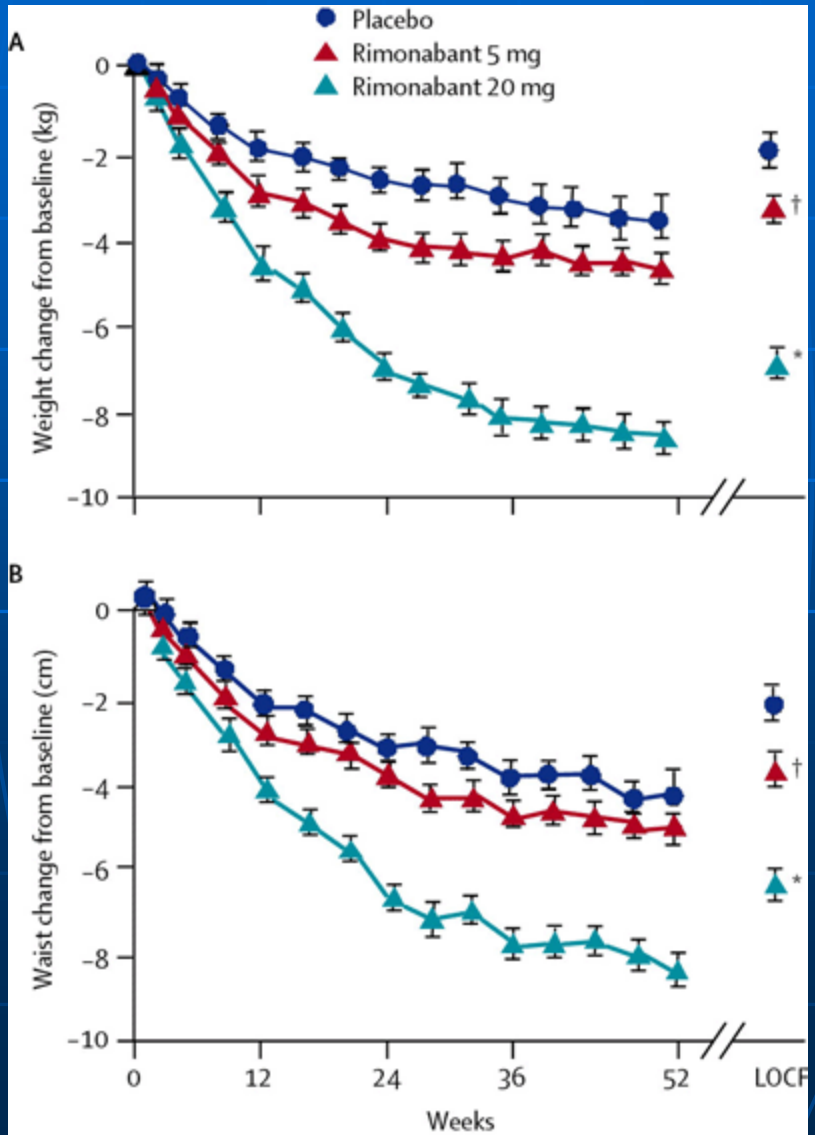
- A selective CB1 endocannabinoid receptor antagonist indicated for the treatment of obesity – 33% of people in the trials lost > 10% body weight (another 33% lost 5%)
- Reduces hunger
- Helps stop smoking
- May reduce alcohol cravings

CB_1 Blockers - Sites and Mechanisms of Action



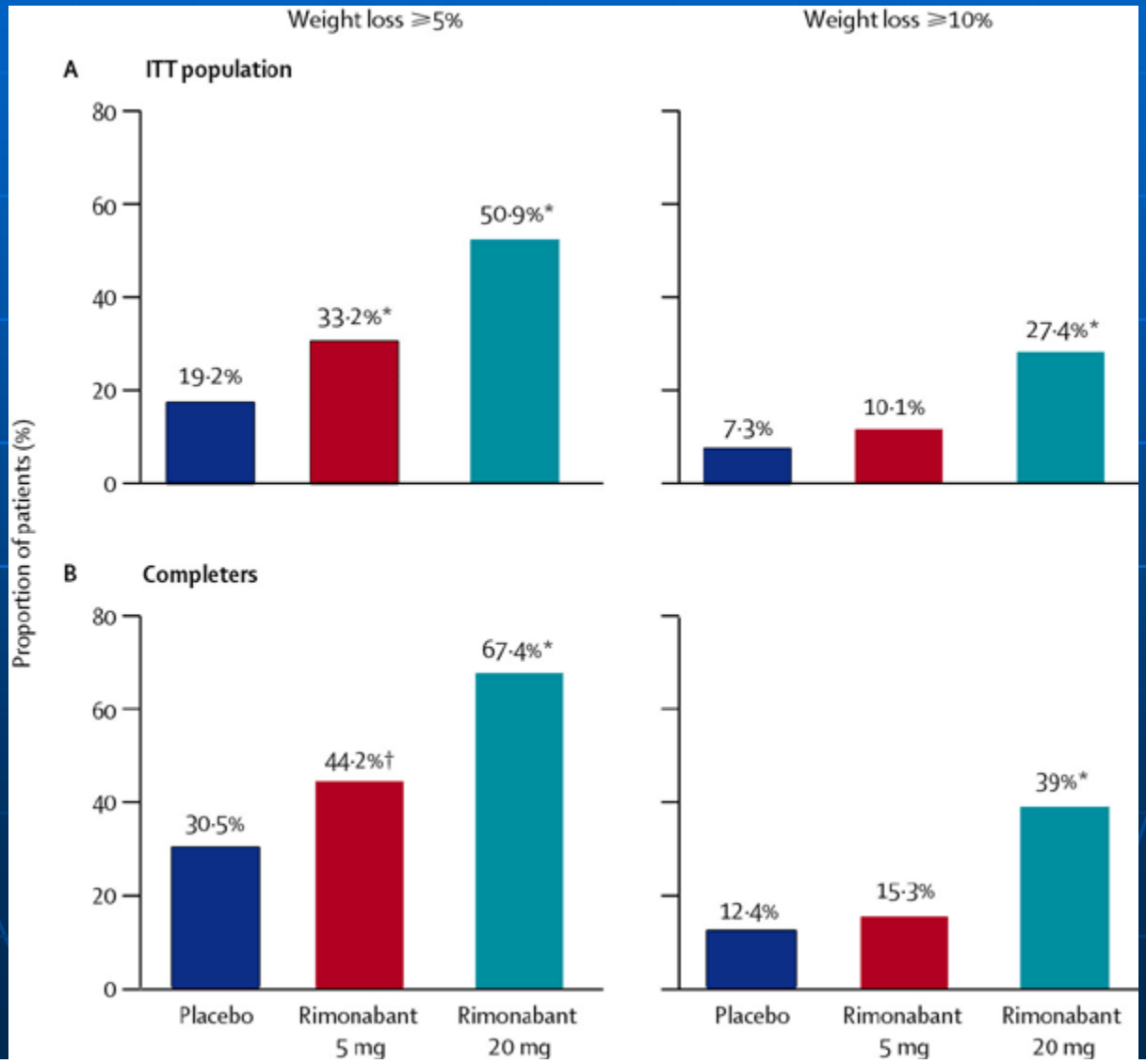
Pagotto et al Lancet 2005;365:1363-4

CB_1 Blockade - Effects on Weight and Waist Circumference



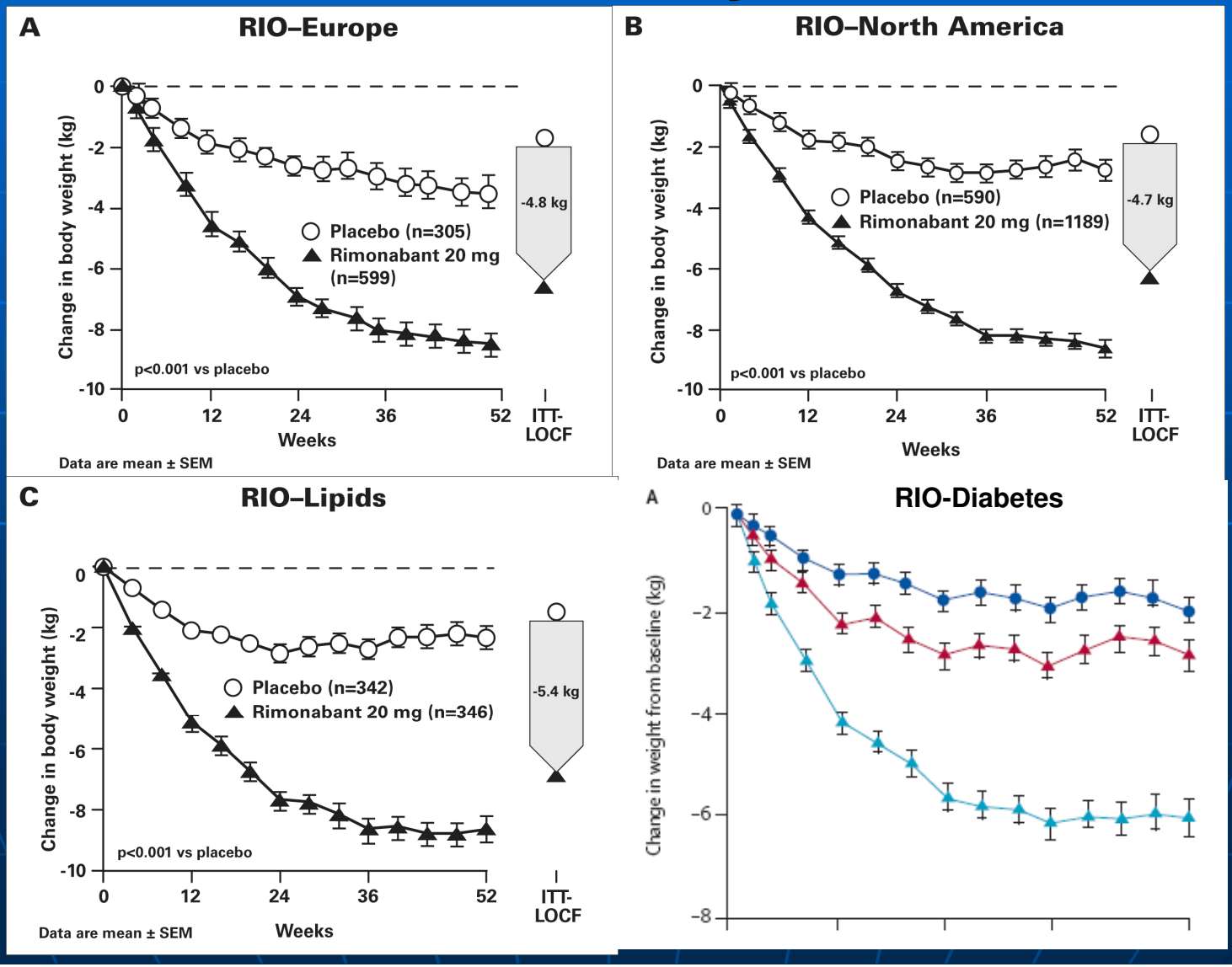
Van Gaal et al Lancet 2005;365:1389-97

CB_1 Blockade - Effects on Weight Loss

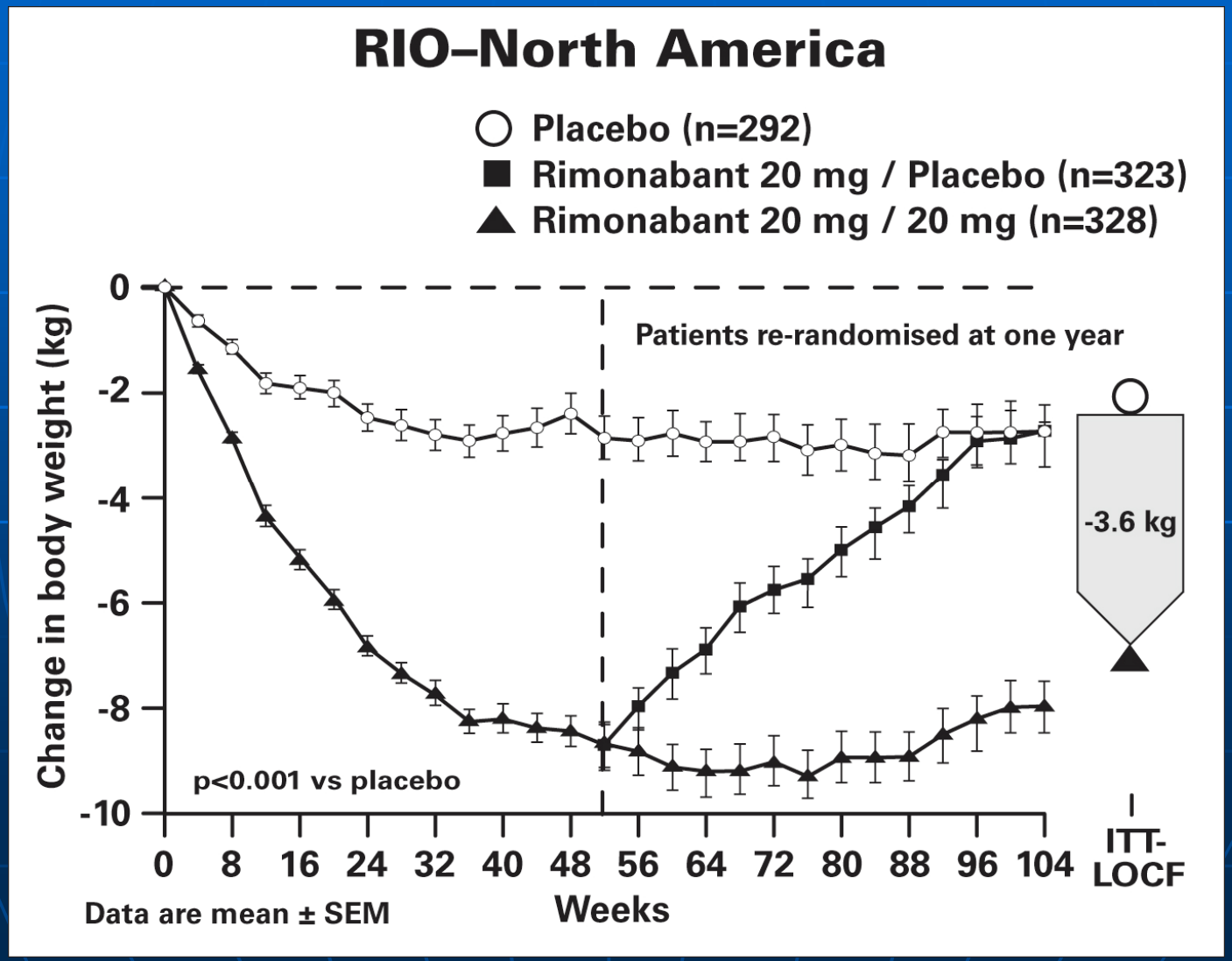


Van Gaal et al Lancet 2005;365:1389-97

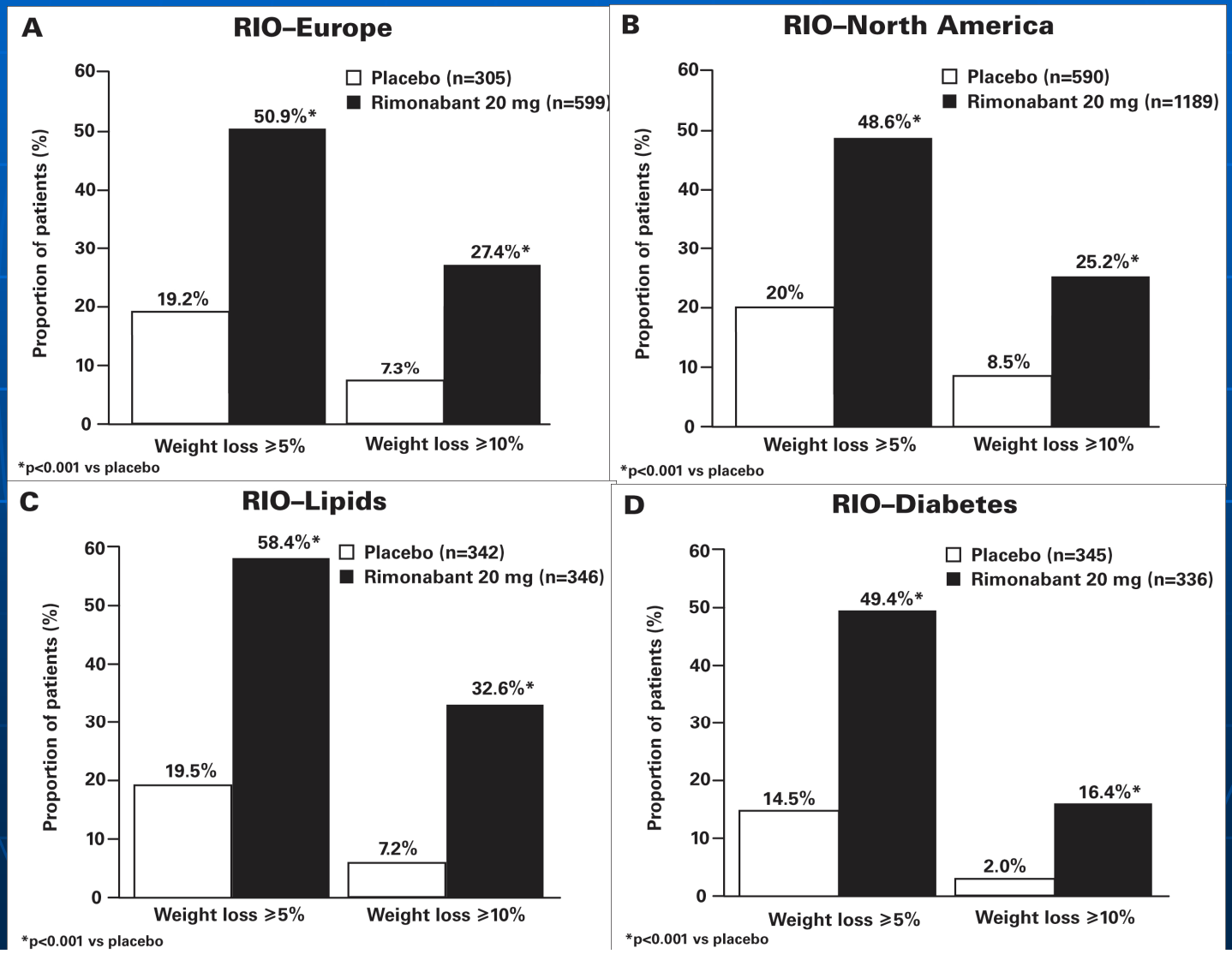
CB_1 Blockade – Effects on Weight Loss at 1 year



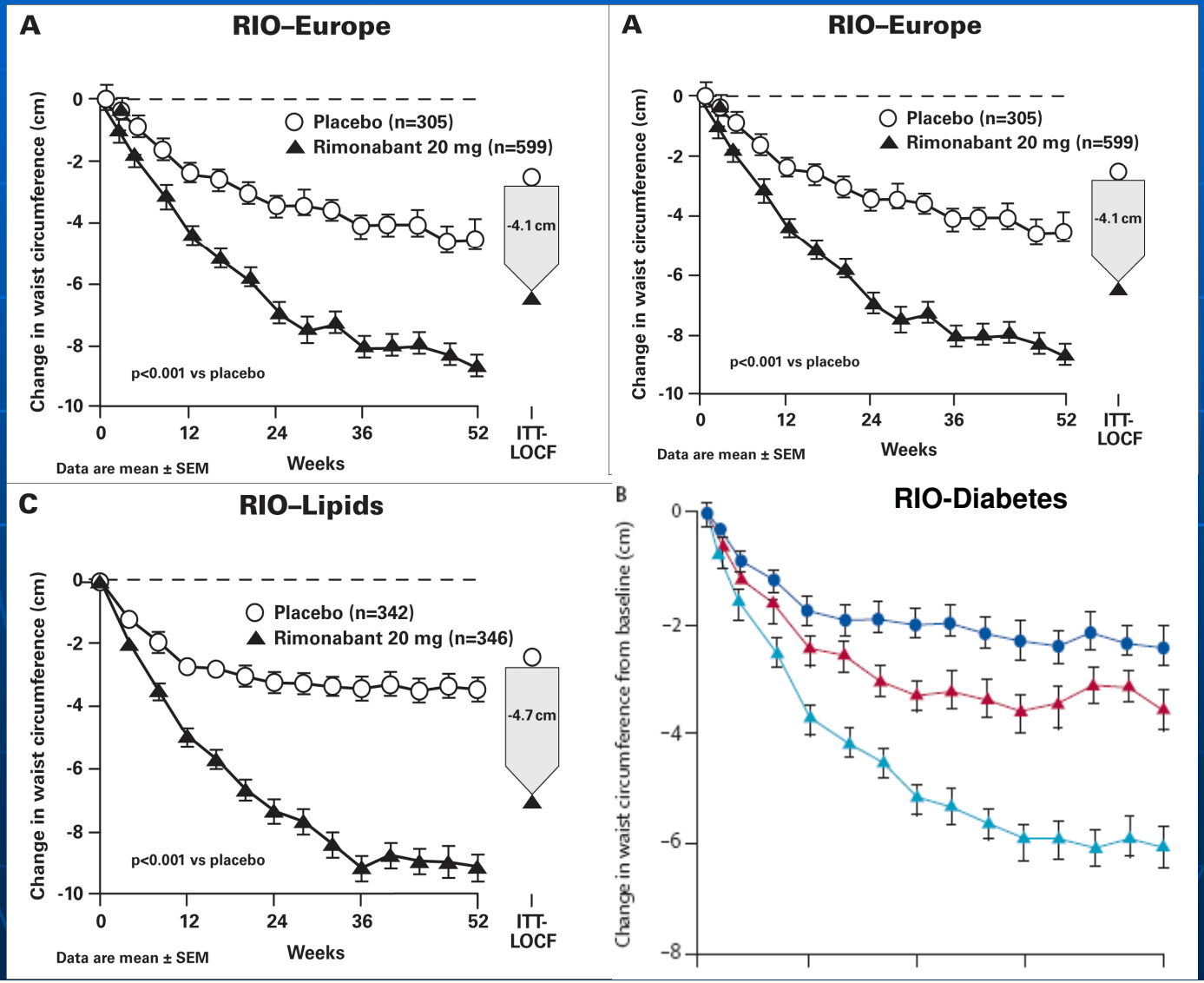
CB_1 Blockade – Effects on Weight Loss at 2 years



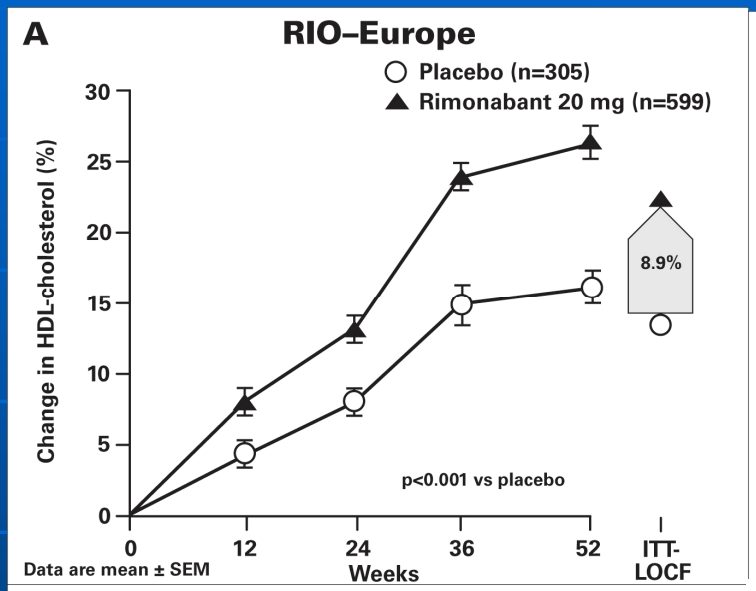
CB_1 Blockade – Proportion of Patients Achieving Target Weight at 1 year

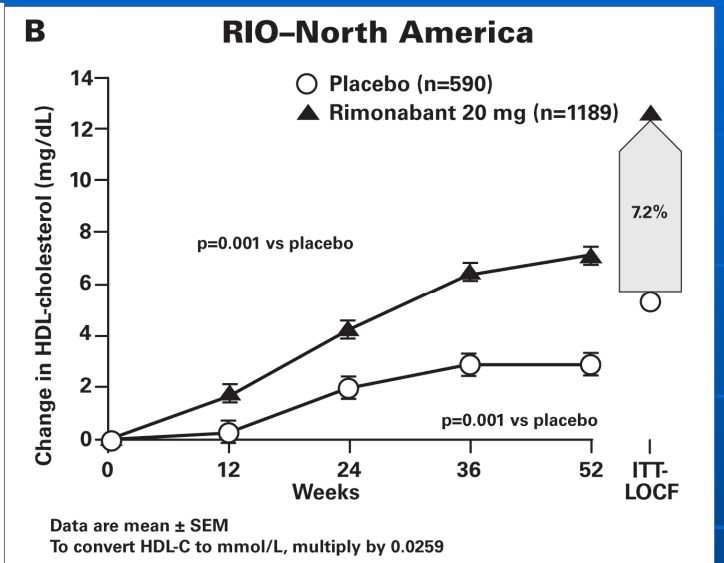


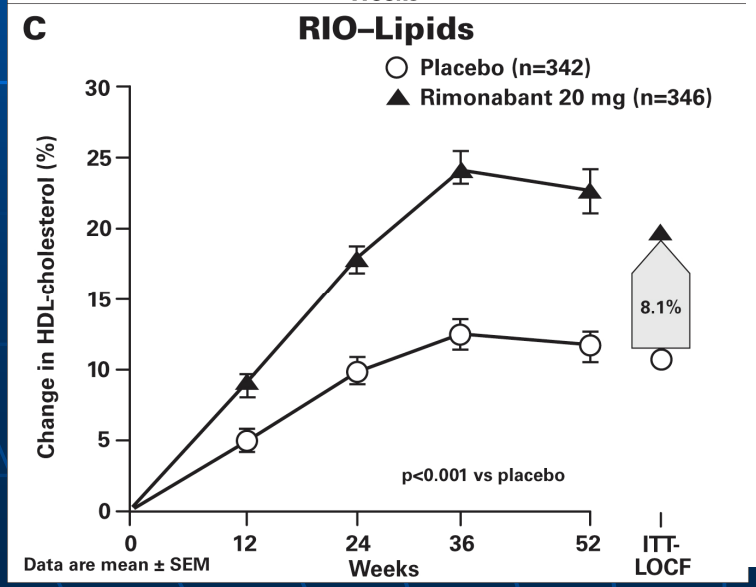
CB_1 Blockade – Effects on Waist Circumference at 1 year

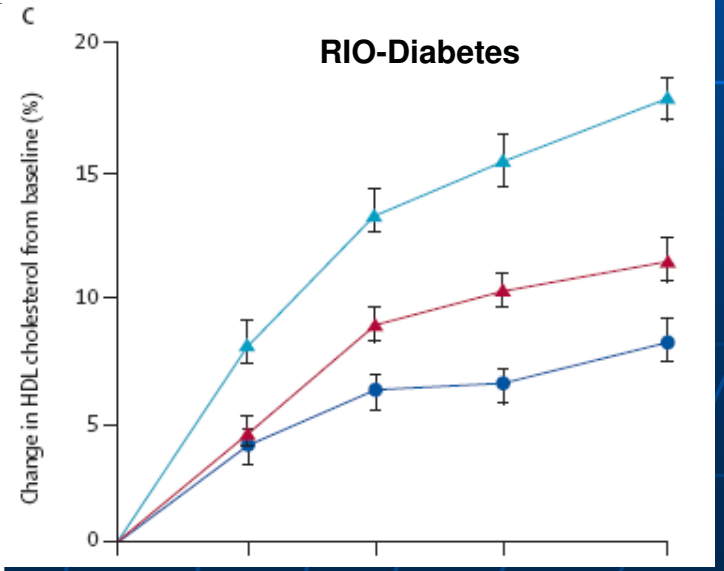


CB_1 Blockade – Effects on HDL at 1 year

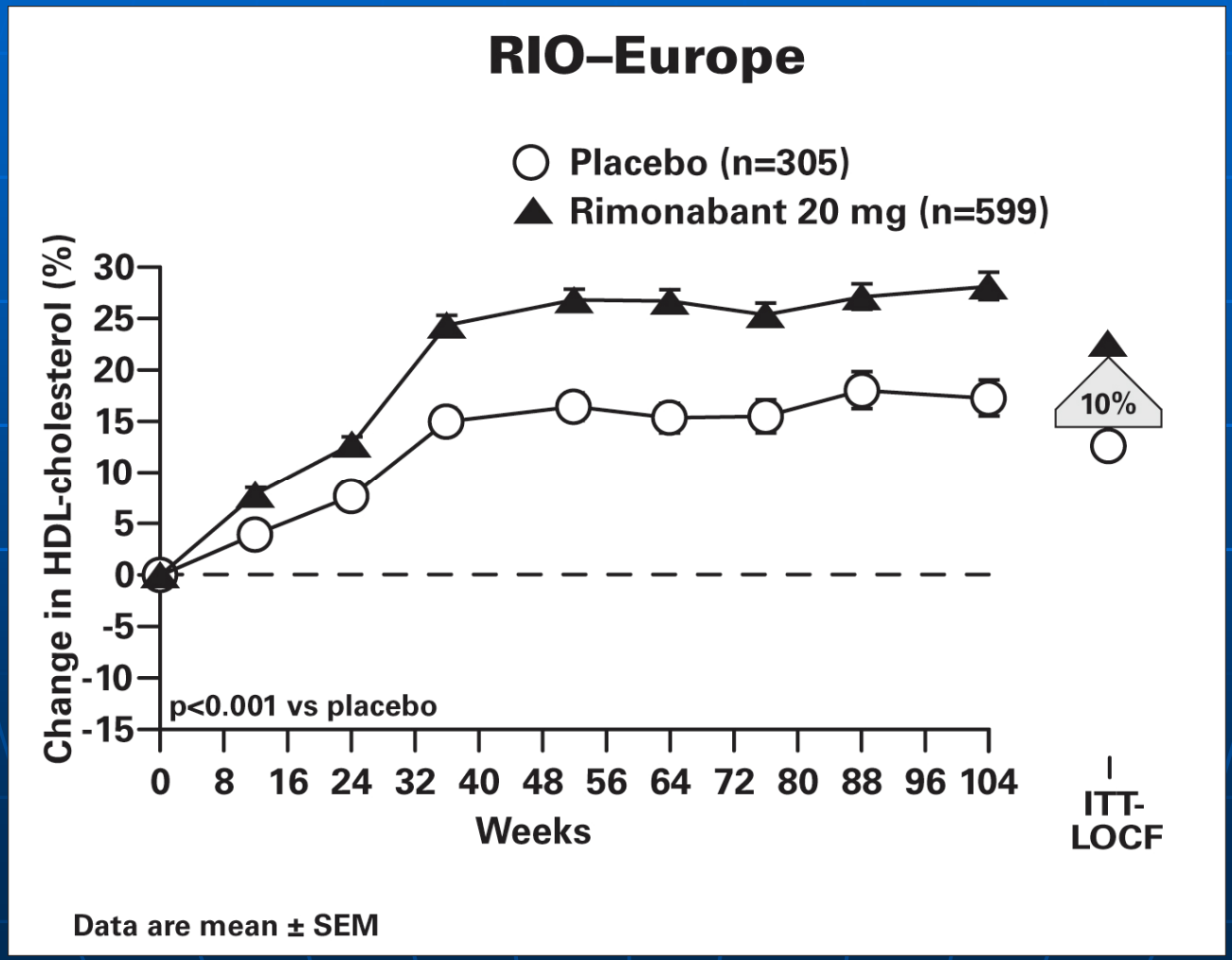




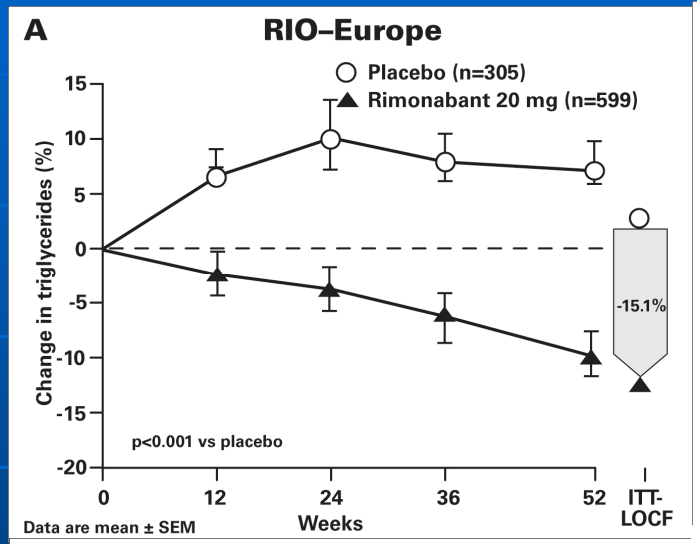


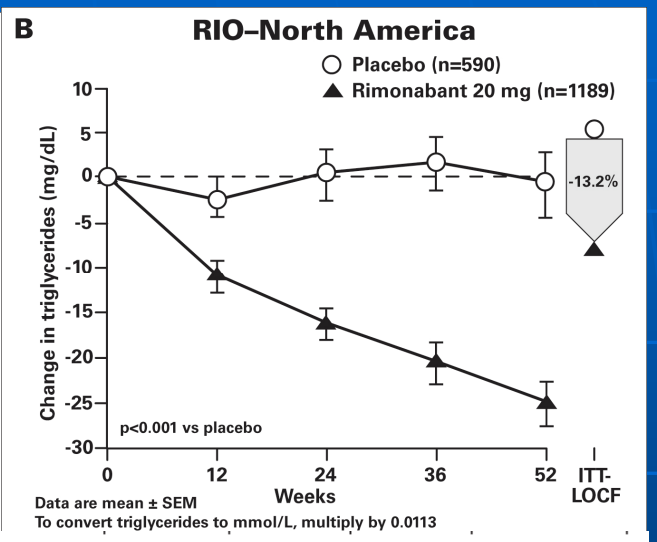


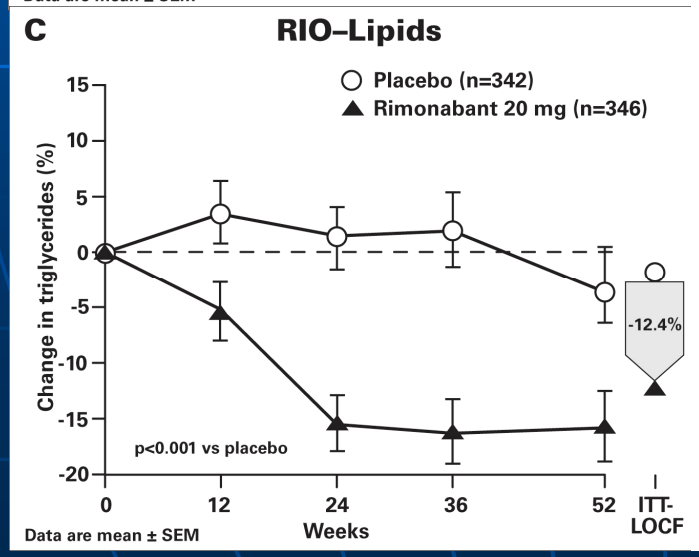
CB_1 Blockade – Effects on HDL at 2 years

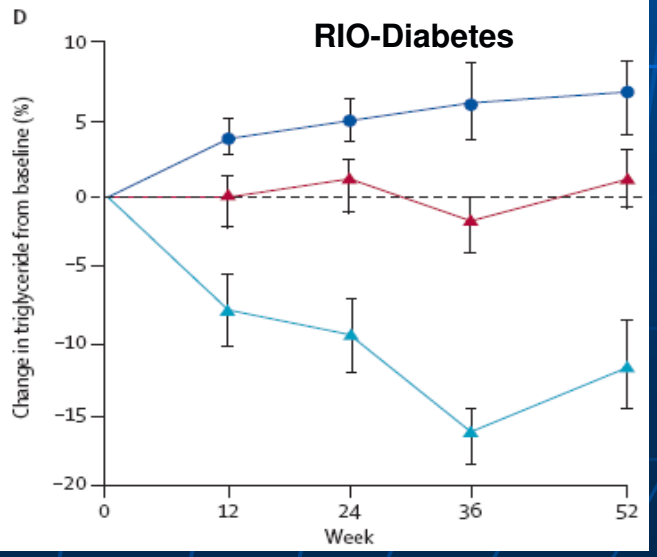


CB_1 Blockade – Effects on TG at 1 year

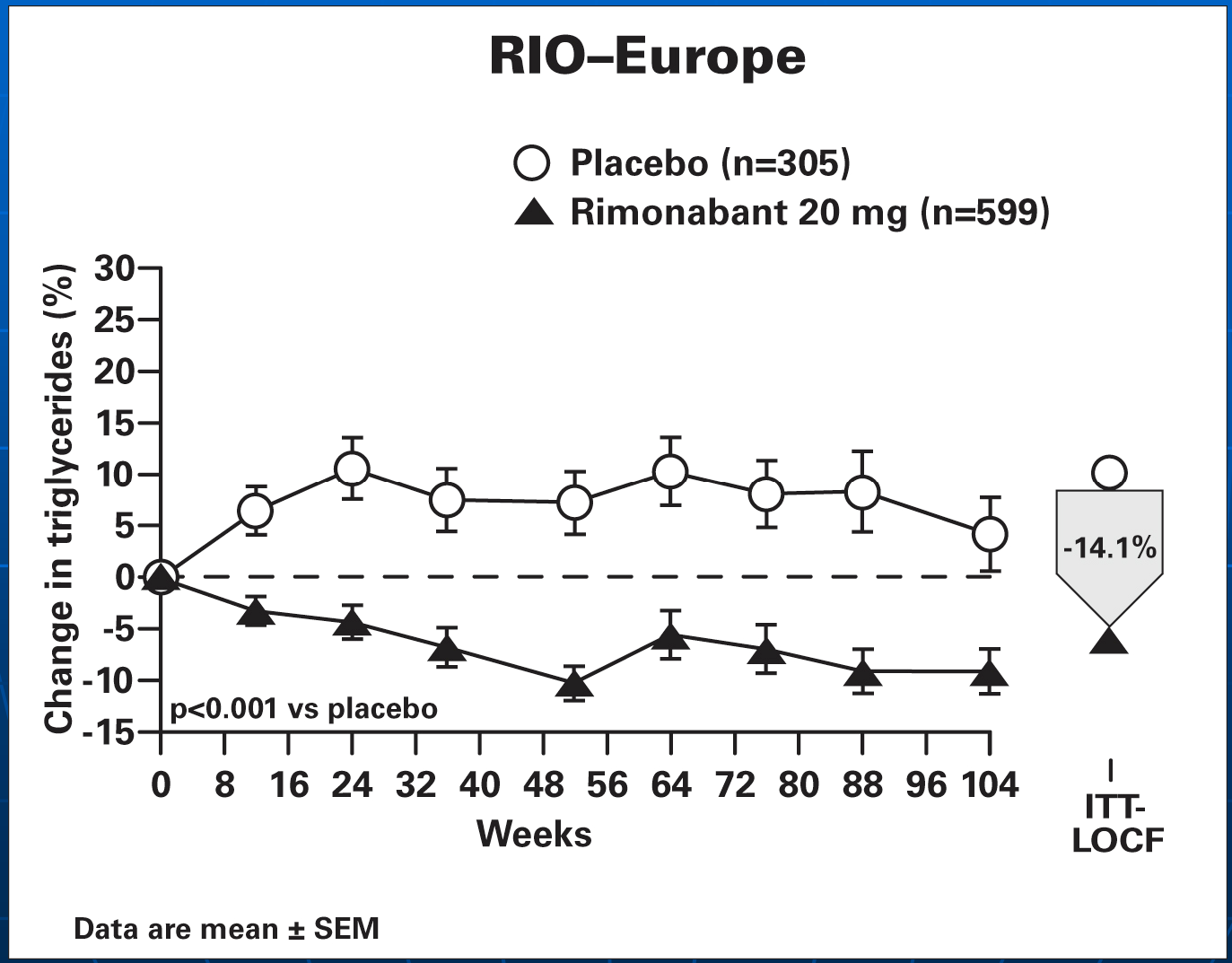




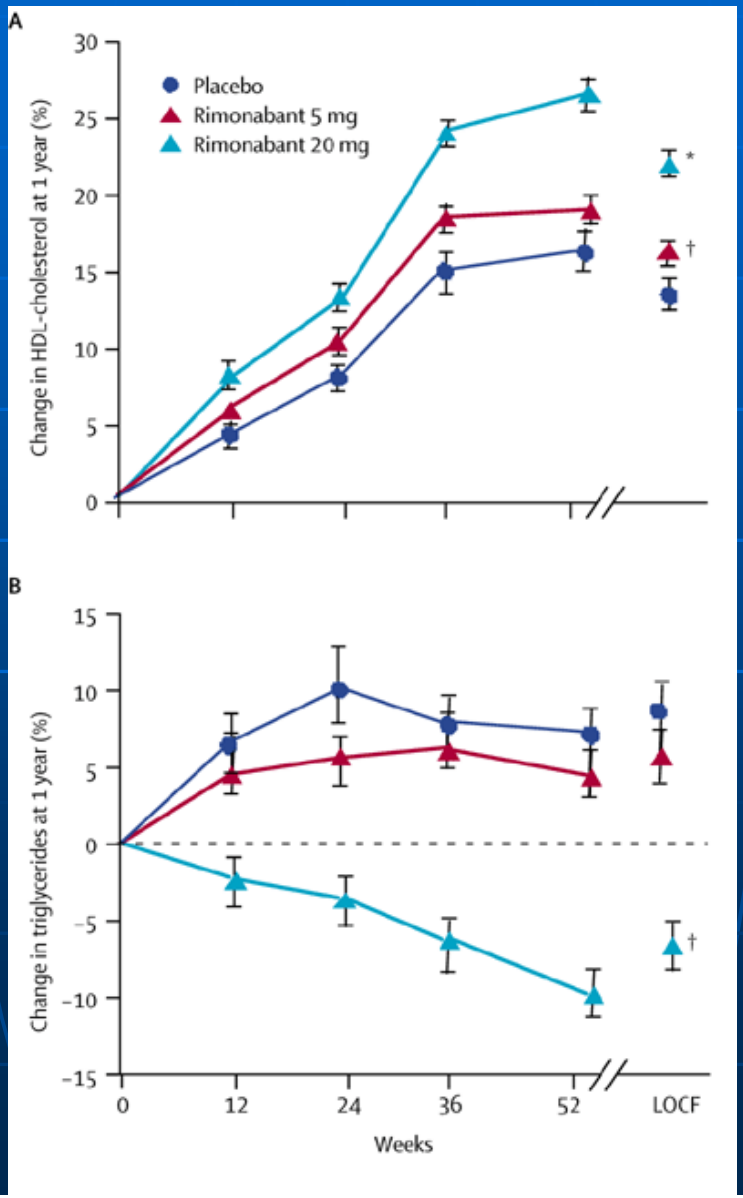




CB_1 Blockade – Effects on TG at 2 years

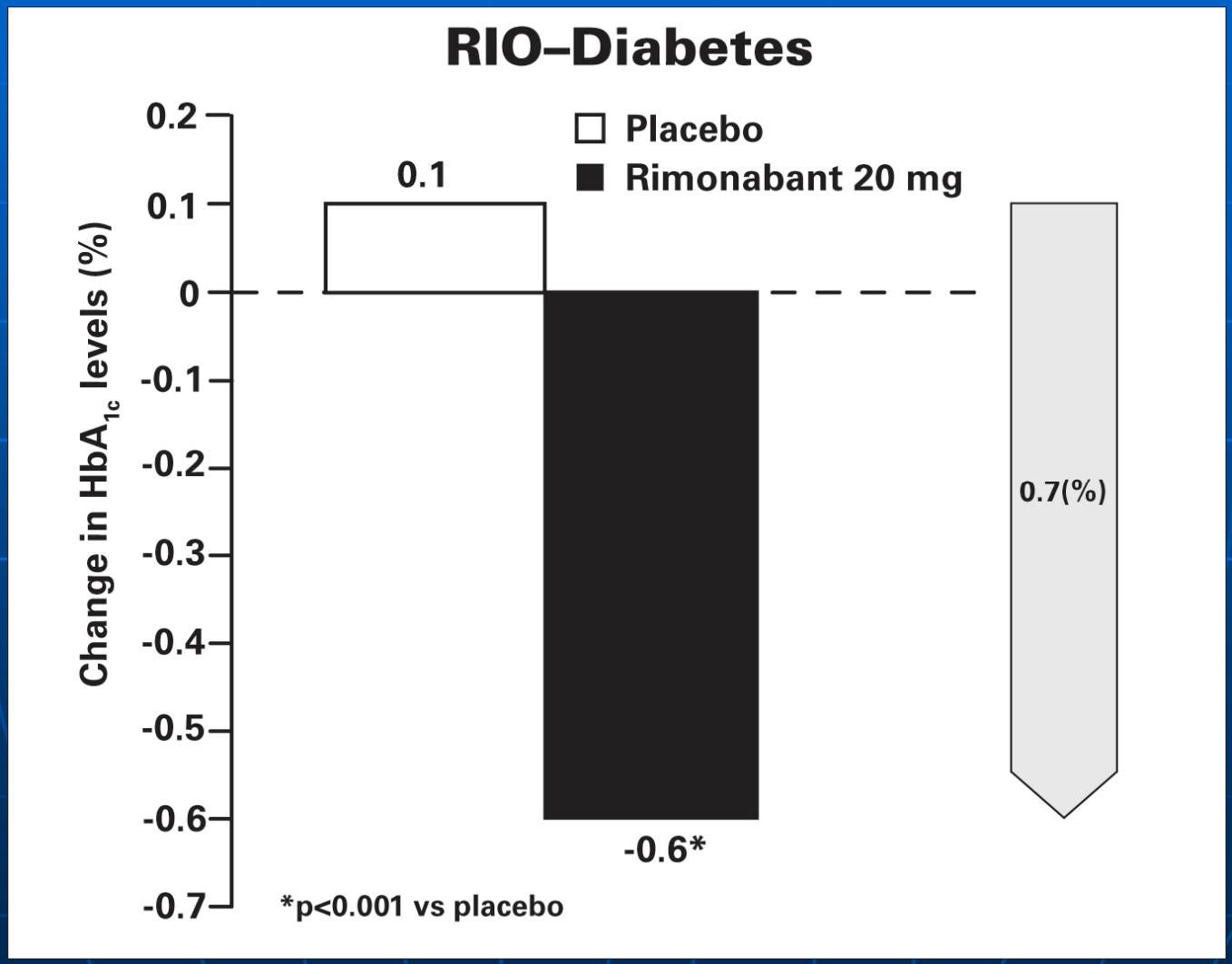


CB_1 Blockade - Effects on Lipids



Van Gaal et al Lancet 2005;365:1389-97

CB_1 Blockade – Effects on HbA_1C at 1 year (2nd line)



Side Effect Profile

	Placebo (n=1603) %	Rimonabant (n=2503) %
Nasopharyngitis	**17.5**	**16.3**
Upper respiratory tract infection	**11.4**	**12.4**
Nausea	**4.9**	**11.9**
Headache	**11.8**	**9.4**
Influenza	**8.6**	**8.9**
Arthralgia	**8.2**	**8.1**
Dizziness	**4.9**	**7.5**
Back pain	**7.6**	**7.0**
Sinusitis	**8.0**	**6.5**
Diarrhoea	**4.8**	**6.3**
Asthenia/fatigue	**5.0**	**6.0**
Anxiety	**2.4**	**5.6**
Insomnia	**3.2**	**5.4**

Adverse events reported at a frequency of >5% in any group.

Ongoing Phase 2 and 3 Trials with Rimonabant

- Smoking cessation
- Alcohol detoxification
- Food craving / eating disorders
- Energy expenditure
- Pre-diabetes / diabetes prevention

Amylin (Pramlintide)

- Synthetic amylin approved by FDA March 2005 for use in type 1 or type 2
- Amylin is made in and secreted from β cells
- Amylin helps suppress glucagon secretion
- sc injection given at mealtimes
- HbA1C reduction of ~0.5%

Ruboxistaurin (Arxxant)

- PKC antagonist
- PKC β is an enzyme that has been implicated in the underlying process of microvascular damage
- For the treatment of diabetic retinopathy, diabetic peripheral neuropathy and macular oedema
- Was due for launch 2006 but safety issues have delayed this

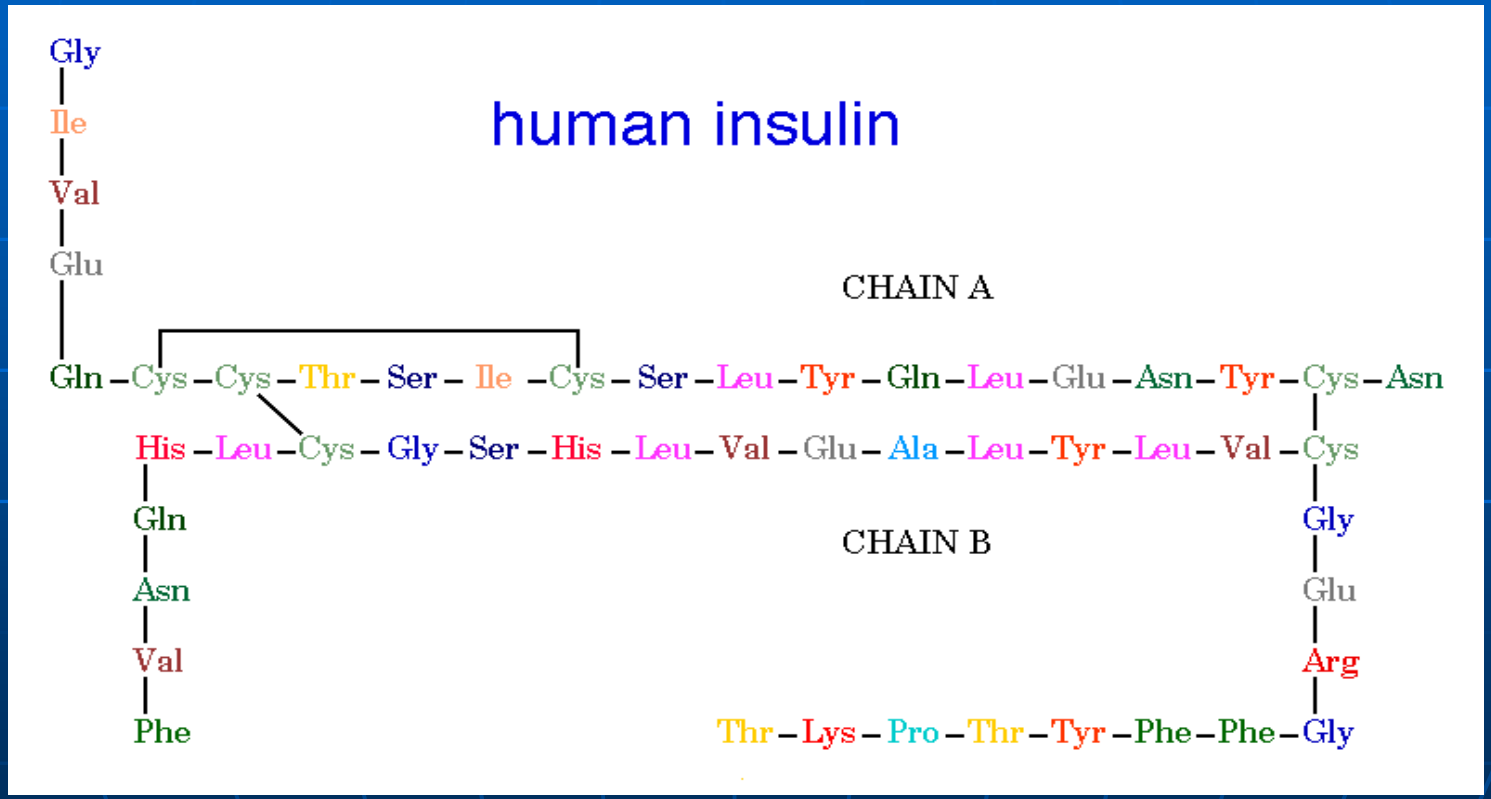
Drugs that can Precipitate or Worsen Diabetes

- Corticosteroids
- β blockers
- ? Thiazide diuretics
- Atypical antipsychotics
- Antidepressants
- Anticonvulsants
- Lithium

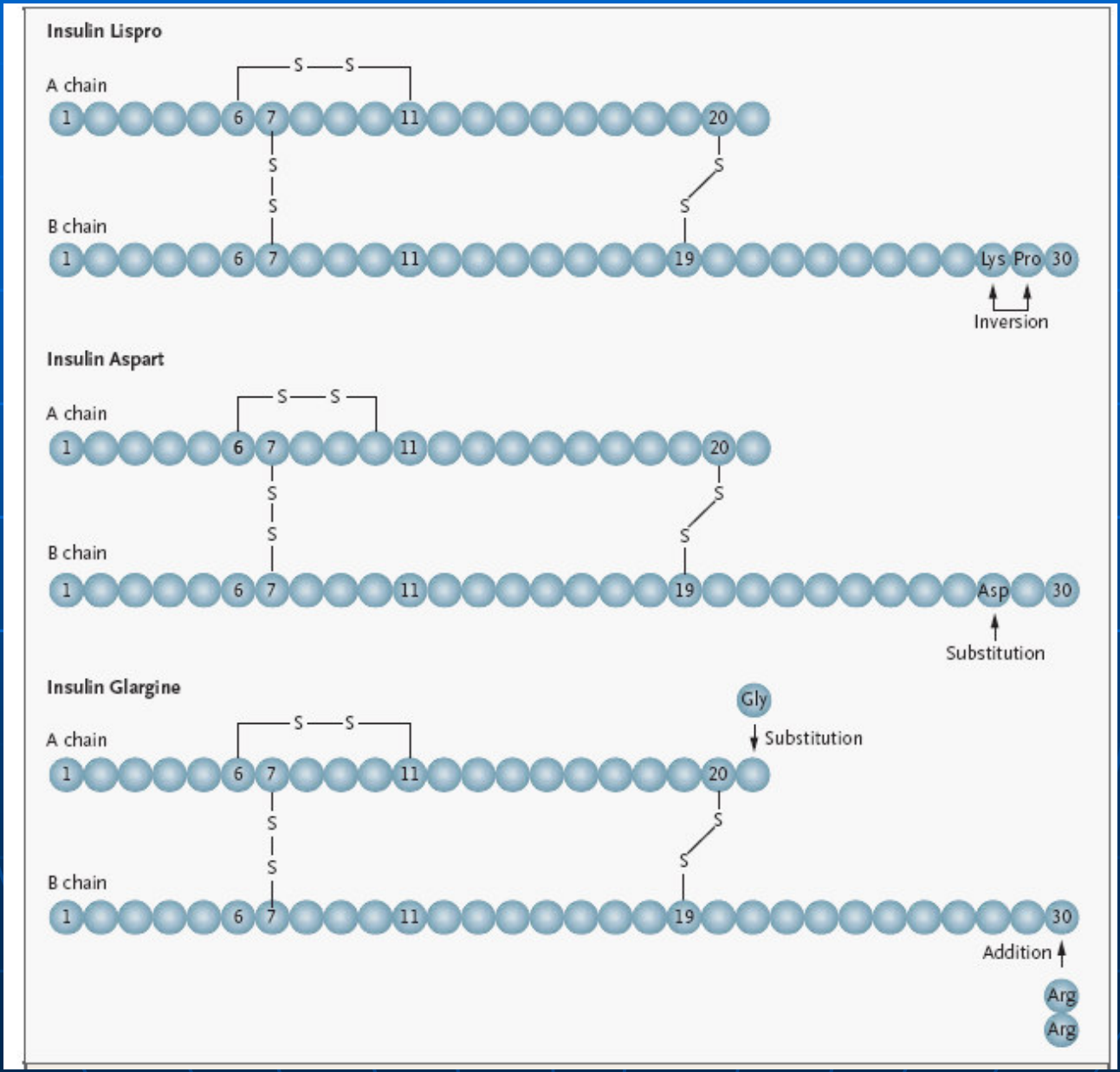
Insulins

- Soluble (short acting)
- NPH (intermediate)
- Once daily
- Mixtures
- Insulin analogues – ultra short, long and mixtures

Insulin

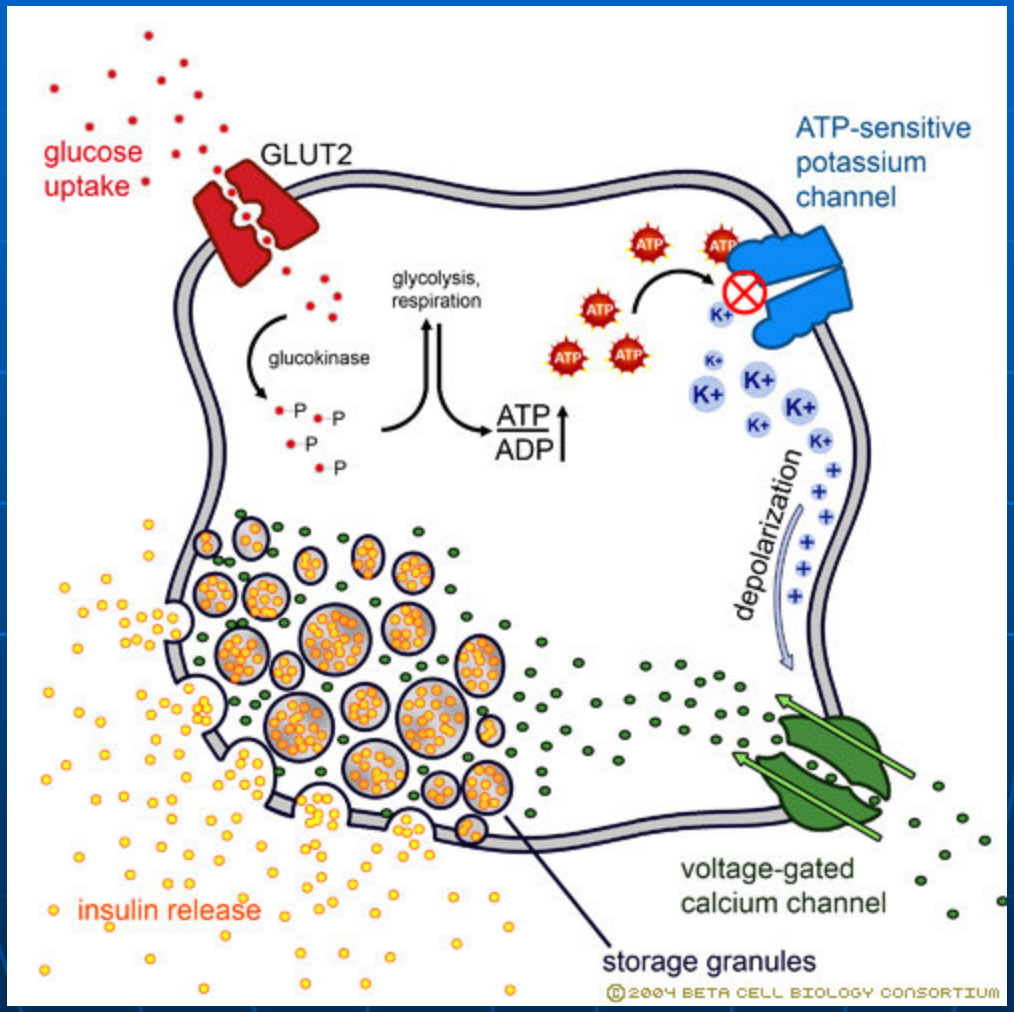

human insulin
CHAIN A
Gly
Ile
Val
Glu
Gln – Cys – Cys – Thr – Ser – Ile – Cys – Ser – Leu – Tyr – Gln – Leu – Glu – Asn – Tyr – Cys – Asn
His – Leu – Cys – Gly – Ser – His – Leu – Val – Glu – Ala – Leu – Tyr – Leu – Val – Cys
Gln
Asn
Val
Phe
CHAIN B
Gly
Glu
Arg
Thr – Lys – Pro – Thr – Tyr – Phe – Phe – Gly

Insulin Analogues



Hirsch NEJM 2005;352 (2):174-183

Beta cell


glucose uptake
GLUT2
ATP-sensitive potassium channel
glycolysis, respiration
glucokinase
ATP
ADP
depolarization
voltage-gated calcium channel
insulin release
storage granules
©2004 BETA CELL BIOLOGY CONSORTIUM

Normal insulin and glucose profiles

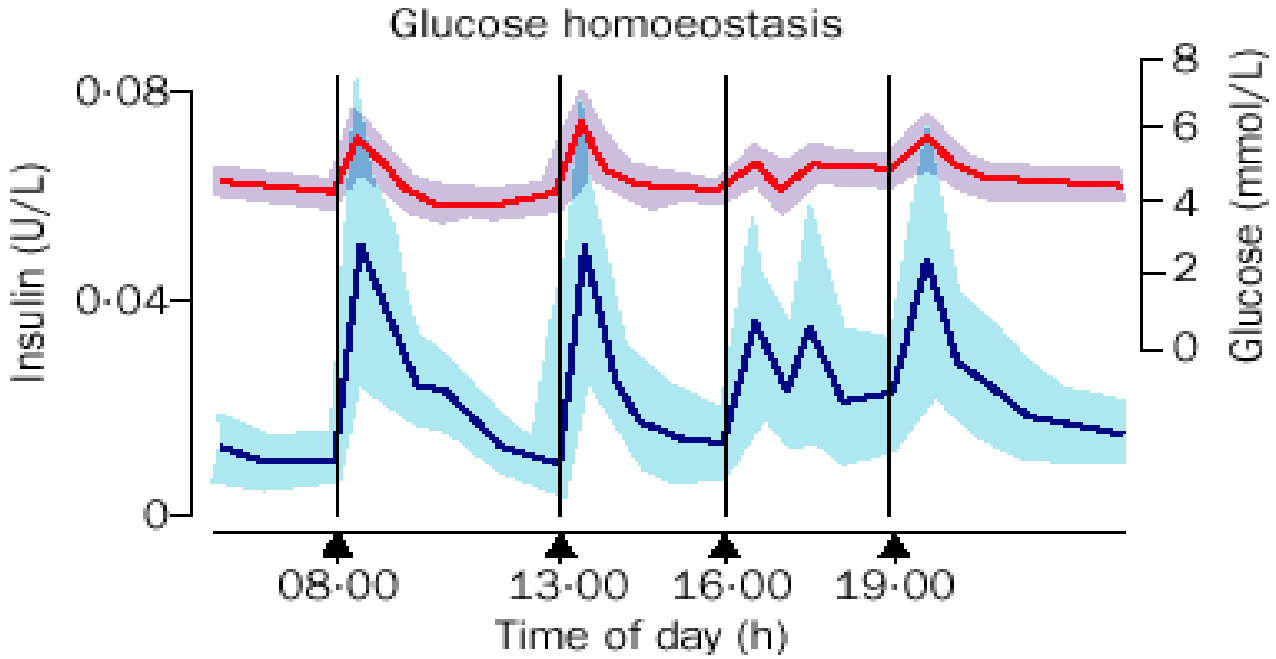
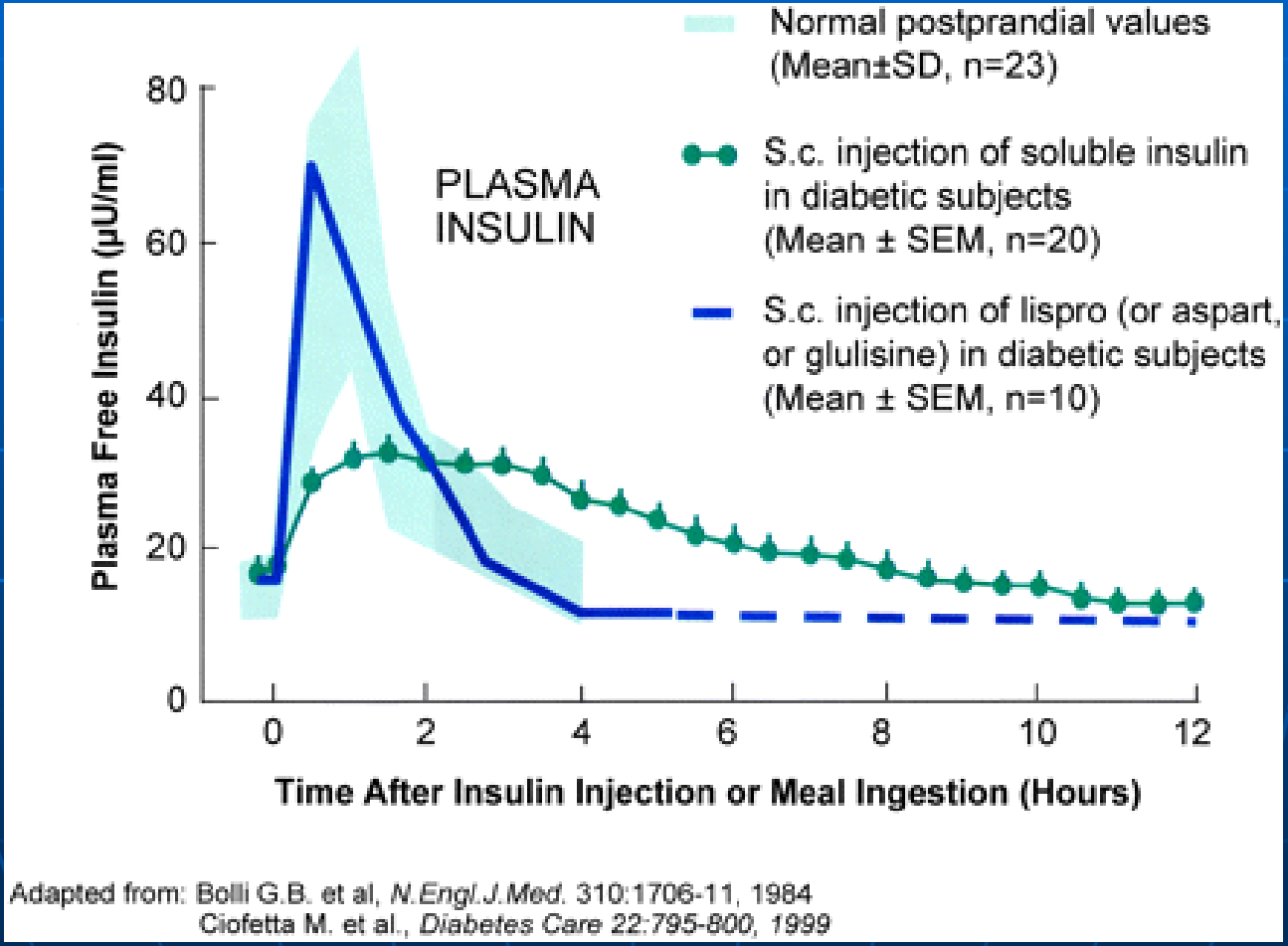


Figure 1: **24-h plasma glucose and insulin profiles in healthy individuals (n=12)**
Mean values with 95% CI.

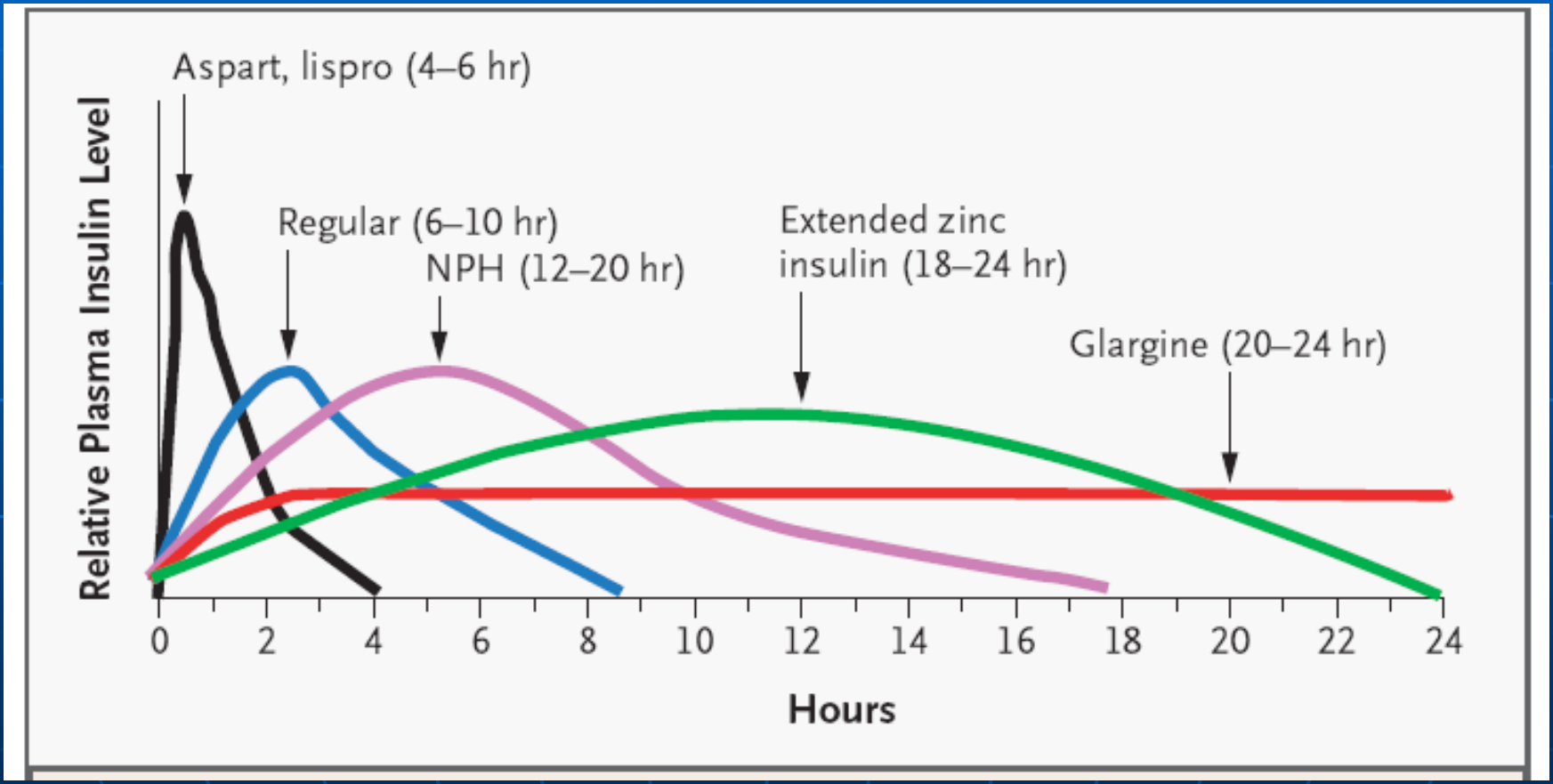
Lancet 2001;358:739

Insulin Profiles



Adapted from: Bolli G.B. et al, *N.Engl.J.Med.* 310:1706-11, 1984
Ciofetta M. et al., *Diabetes Care 22:795-800, 1999*

Insulin Durations



Hirsch NEJM 2005;352 (2):174-183

Short acting

- Actrapid
- Humulin S

NPH

- Insulatard
- Humulin I

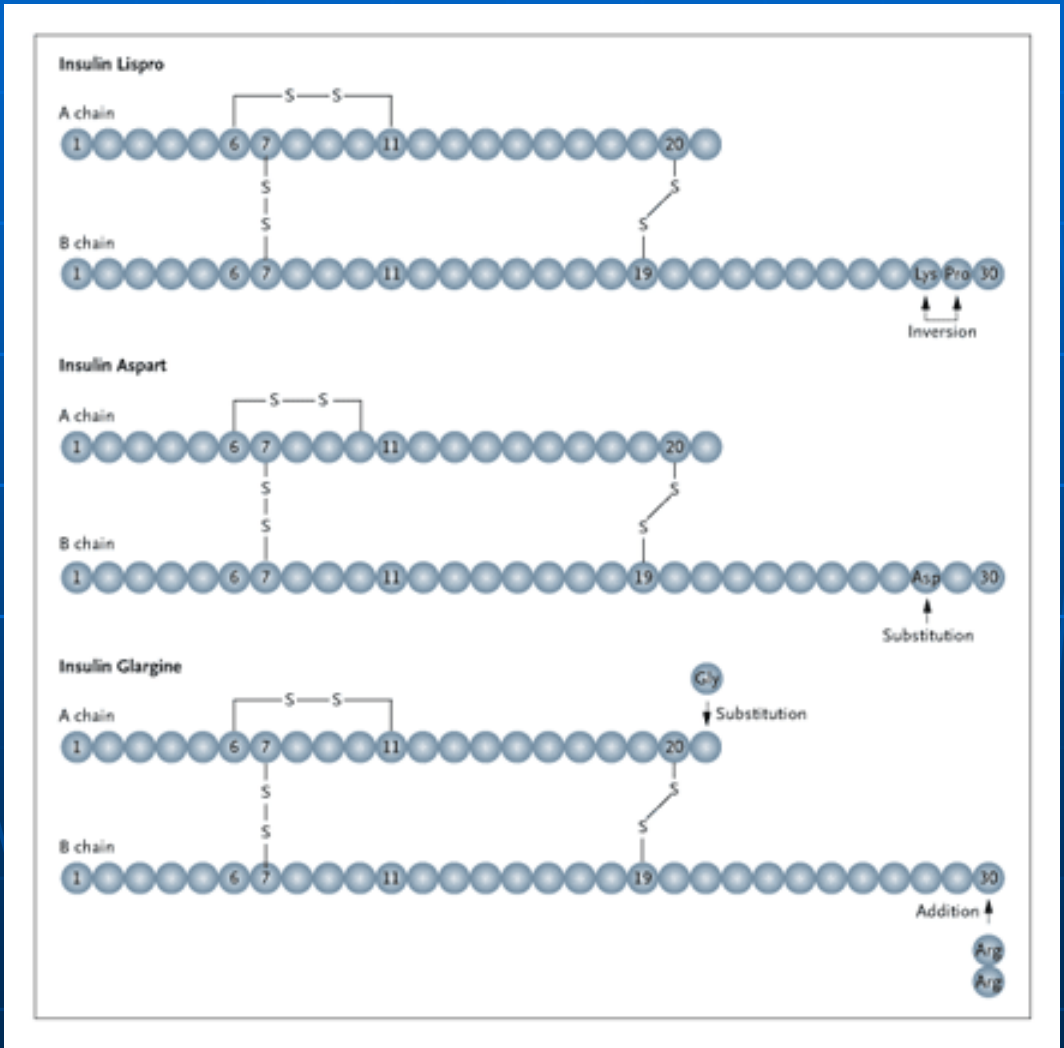
Once daily

- Ultratard
- Monotard
- [Often given with Metformin]
- [Both being withdrawn]

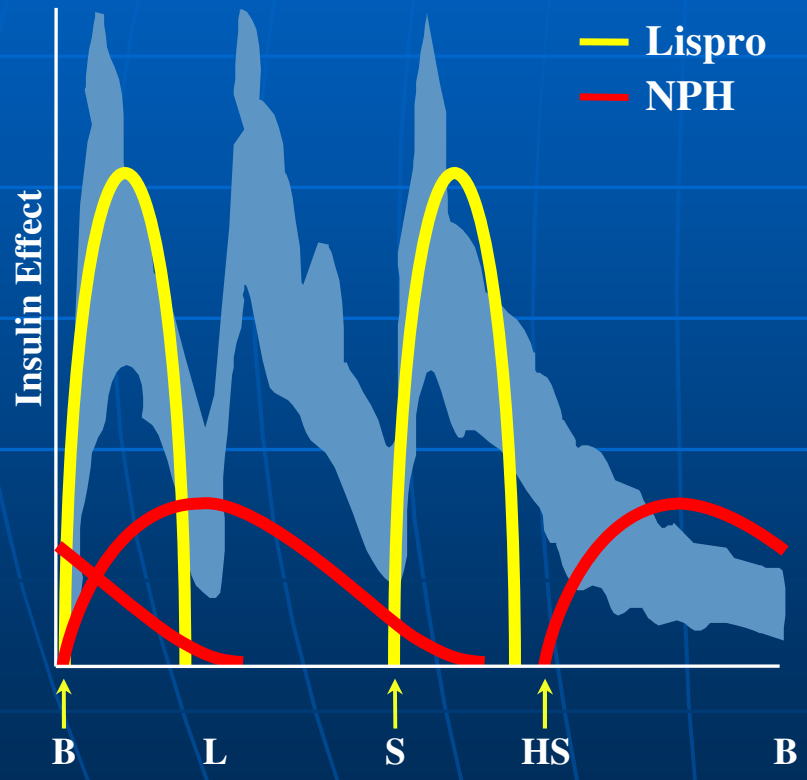
Mixtures

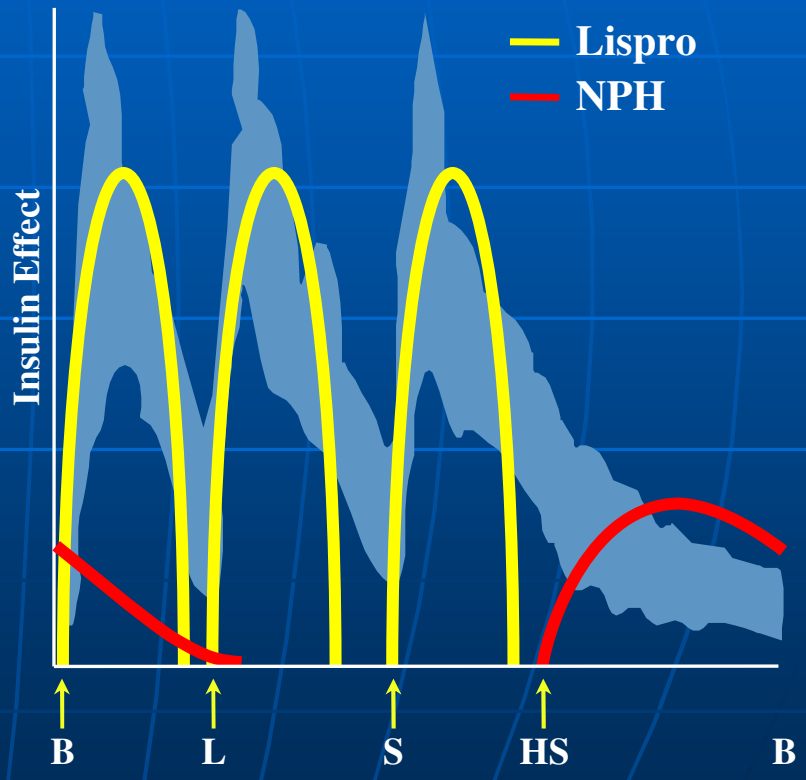
- Mixtard 30
- Humulin M1/M2/M3/M4/M5

Insulin Analogues



Multiple Daily Injections (MDI)
NPH + Mealtime Lispro





Analogues

- Ultra short acting
  - Novorapid (Insulin Aspart)
  - Humalog (Lispro)
- Mixtures
  - Humalog 25
  - Novomix 30
- Long acting
  - Insulin Glargine
  - Detemir

Recent Data

Cost-effectiveness of insulin analogues for diabetes mellitus

Chris G. Cameron MSc, Heather A. Bennett BPharm PhD

Interpretation: The cost-effectiveness of insulin analogues depends on the type of insulin analogue and whether the patient receiving the treatment has type 1 or type 2 diabetes. With the exception of rapid-acting insulin analogues in type 1 diabetes, routine use of insulin analogues, especially long-acting analogues in type 2 diabetes, is unlikely to represent an efficient use of finite health care resources.

CMAJ 2009:180(4):400-407

Any questions?